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TABLE OF CONTENTS ON 3rd COVER

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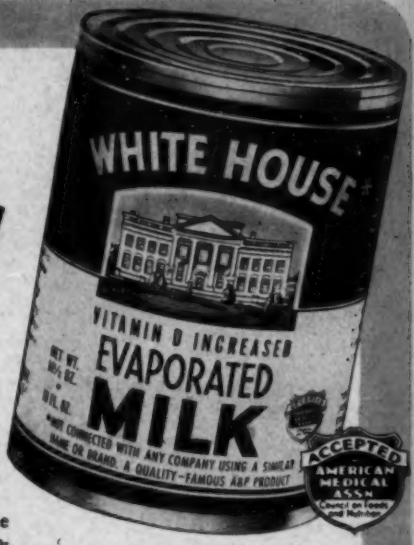

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The Journal of Pediatrics

VOL. 25 NOVEMBER, 1944 No. 5

Original Communications

A REVALUATION OF THE PNEUMONIAS OF INFANCY

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ACUTE respiratory infections in infants present the physician with some of his most challenging problems. The anatomic and physiologic immaturity of the pulmonary system undoubtedly plays a special role in the development of pneumonia in infancy. Next to those of the upper respiratory tract, infections of the lungs are the most inaccurately described from the viewpoints of etiology and pathogenesis. One of the purposes of the present communication is to remove certain forms of pneumonitis from the wastebasket of "bronchopneumonia." The development of more accurate diagnostic procedures has so enlarged the field that the pathologico-anatomic classification no longer suffices to delineate the various clinical entities now known to exist. An etiologic and pathogenic grouping offers a more nearly accurate appraisal of a disease which is not infrequently due to multiple inciter agents. There is ample evidence to suggest that many of the agents act synergistically or in concert to produce the picture of pneumonia as seen in infancy. Study of specific histopathologic changes in the lungs has clarified much of the confusion and has frequently given the final answer to the correct diagnosis of such "mixed pneumonias."

Advances in our knowledge regarding pathogenesis and a better understanding of the anatomy and physiology of the infant's pulmonary system as they relate to the development of pneumonia have proved to be of considerable aid in the prevention and treatment of many of these diseases. Strict isolation of the infant with predisposing and precursor diseases, immunotherapy, chemotherapy, and oxygen administration constitute resources available for these purposes.

PATHOGENESIS

The importance of aspiration or gravitation of bacteria-laden fluid from the upper respiratory passages into the lungs has only

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recently come to be fully appreciated as a cause of pneumonia. Experimental studies by Robertson[1] on dogs have demonstrated that the escape of infected fluid exudate from the upper respiratory tract beyond the epiglottic barrier plays a much more important role in the inception of pulmonary infection than does the inhalation of bacteria-laden droplets from the atmosphere. Kneeland and Dawes[2] found an increase in pneumococci in nasal cultures after the common cold. Webster and Clow[3] likewise found that during the course of a cold the bacteria increased markedly in the upper respiratory passages. Infants can harbor pathogenic pneumococci (for example, type XIV) for some time without developing symptoms of pneumonia until attacked by an upper respiratory infection, according to recent studies reported by Smillie.[4] Dochez and associates[5] showed that the common cold is caused by filtrable agents which greatly increase the activity of potential bacterial pathogens. The latter are undoubtedly responsible for the severe diseases so frequently associated with the common cold.

Robertson[1] listed certain conditions as being essential for the production of the pneumonic lesion: first, the implantation of pneumococci in the terminal airways; second, a fluid but viscous medium which prevents their rapid expulsion from the region of the lung; and third, the presence of local irritation. The common cold and related virus infections of the respiratory passages are the commonest predisposing and precipitating causes of pneumonia because they produce the congestion, edema, and local irritation so essential to the inception of pneumonia. These factors are even more potent in the infant, whose respiratory passages are small and immature in their development. The importance of preventing the infected exudate, which is so commonly associated with the upper respiratory diseases, from gravitating or being aspirated into the lower respiratory passages thus becomes evident.

The consequence of the gravitation of bacteria-laden exudate as opposed to the inhalation of infected droplets from the atmosphere should not lead us to overlook the importance of aerial transmission of disease. It has been established in the case of influenza; and few would doubt that the common cold, measles, and probably many of the atypical pneumonias now so prevalent are the result of air-borne infection. The importance of preventing these diseases becomes evident when it is appreciated that they are for the most part the precursors of pneumonia. Ultraviolet light was found by Sommer and Stokes[6] to be effective in reducing the number of air-borne organisms in a hospital ward. Recent progress in the field of aerosols offers considerable hope for prevention, especially in nurseries and infant wards where the rapid spread of infection can be a most serious problem. Robertson and associates[7, 8] have demonstrated the lethal effect of propylene glycol and triethylene glycol vapors on air-borne bacteria and influenza virus. Henle and associates[9] have also reported propylene glycol vapor as an effective disinfectant of the air in a large hospital ward. Loosli and associates[10] have

recently reported that the infectivity rate for mice was much higher in an atmosphere with low relative humidity (23 per cent) than in one with high relative humidity (89 per cent).

PREVENTION AND TREATMENT

The newer knowledge regarding the development of experimental pulmonary infections has led to some practical applications in preventing pneumonia, especially in infancy. For example, much can be accomplished toward this end by the employment of proper posture alone. The backward slope of the trachea and bronchi is an important anatomic relationship and appears to have considerable significance in this connection. When the infant is placed flat on his abdomen, the angle, which the trachea and main bronchi make with the ventral surface of the body, is approximately 20 degrees. In Fig. 1 the backward angle of

Fig. 1.—A planigram (body section roentgenogram) of the lung showing the slope of the trachea and main bronchi with respect to the ventral surface of the body.

these structures is illustrated in a lateral body section roentgenogram of the lung of a 6-month-old infant. By elevating the foot of the crib, the angle between the pulmonary passages and the horizontal plane can be increased by from 10 to 15 degrees. The prone position is tolerated well by babies and many seem to prefer it. The mattress under the infant should be firm and flat, allowing free movement of the head to one side or the other (Fig. 2).

The mechanisms for the removal of foreign material from the lung are quite adequate in the normal subject, with the possible exception of prematurely born and very young full-term infants. Robertson[1] states that the lungs of normal human beings are for the most part kept sterile. The commonly recognized methods of elimination of particulate materials and fluids from the lung are cough, ciliary and muscular action in the trachea and bronchi, and phagocytosis in the alveolar

Fig. 2.—A 6-month-old infant showing the prone position and postural drainage. The bed is elevated at the foot about 12 degrees.

spaces. Unfortunately, in the infant some of these mechanisms are immature and less efficient in removing material from the lung. Our studies in infants have shown that the development of cilia may be incomplete or absent in bronchioles with diameters of 0.75 mm. or less. Miller[11] showed sections from adult lungs with ciliated cuboidal epithelium in bronchioles as small as 0.35 mm. in diameter. This difference assumes even greater significance when it is recalled that the infant's lung, while much smaller in the gross, is relatively larger in its microscopic parts. Fig. 3 shows the relative sizes of the *sacculi alveolares* from *A*, a 9-week-old infant; *B*, a 14-year-old child; and *C*, an adult 38 years of age.

In the *normal* experimental animal, Boyd and associates[12] showed that postural pulmonary drainage does not increase the output of respira-

tory tract fluid. However, when the ciliated mucosa lining the trachea is damaged, the output of fluid is doubled or tripled by postural drainage. When the tracheobronchial mucosa is normal, greatly increased amounts of fluid can be handled. They conclude that cough is not likely to be useful and productive unless there is extreme damage to the tracheobronchial mucosa or unless the cilia are bathed in a nonphysiologic medium, such as pus. Postural drainage is likely to have the same limitations.

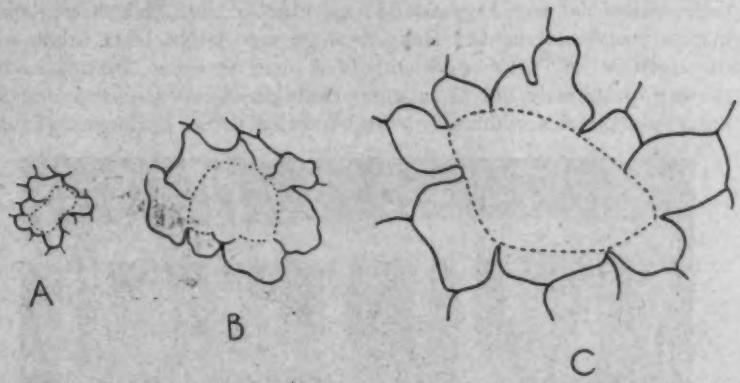

Fig. 3.—These outline drawings illustrate the change in size of the sacculi arising from growth and increased activity of the lung. *A*, from a child 9 weeks old. *B*, from a youth 14 years old. *C*, from an adult 38 years old. All drawn under the same amplification. (×50.) (From Miller: The Lung, Springfield, Ill., 1937, Charles C Thomas.)

Recent experimental studies by Nungester and Klepser[12] showed that the epiglottic barrier is incomplete, particularly in chilled animals as opposed to controls kept at normal atmospheric temperatures. Alcohol and ether anesthesia produced an effect similar to that of chilling. These findings add further to the importance of any practical means for preventing infected material from reaching the lower respiratory passages. Robertson[1] has called attention in particular to the importance of postural drainage in the prevention of postoperative pneumonia. The prone position might also be helpful in preventing postoperative atelectasis, particularly if combined with elevation of the foot of the bed.

Asphyxia as a cause of excessive aspiration of amniotic fluid or vaginal secretion at the time of birth cannot be overemphasized. It plays a very significant role in the development of congenital or neonatal pneumonia. In the infant subjected to asphyxia, therefore, as in the postoperative patient, postural drainage may be most significant as an adjunct to prevent or to treat this condition. According to MacGregor,[14] asphyxia produces pulmonary congestion and edema, as well as depresses the respiratory center, and thereby adds immeasurably to the problem of pneumonia in the newborn infant. The avoidance of asphyxia neonatorum is thus of vital importance in preventing congenital

aspiration pneumonia. From this viewpoint, prompt use of oxygen in the treatment of asphyxia is essential.

The problem of sudden death in infants previously thought to be well ("crib death") has not as yet been completely solved. However, there is considerable evidence to indicate that pneumonia may be responsible for death in many such cases.[15-18] It is interesting to speculate on what effect the prone position might have in their prevention. For some time, we have made a practice of placing infants in the newborn nursery on their abdomens, and have advised mothers to have their babies sleep in this position at home. Many mothers report that their babies will not sleep in any other position. If allowed to do so, infants in the nursery voluntarily flex their legs and thighs, frequently assuming the knee-chest position which promotes tracheobronchial drainage (Fig. 4).

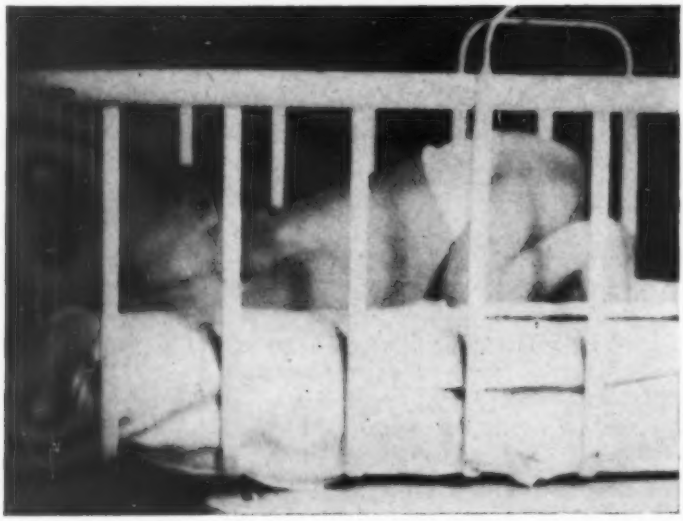

Fig. 4.—A newborn infant in the prone position with the legs flexed on the abdomen, increasing the angle of tracheobronchial tree with the horizontal.

This posture closely resembles that assumed during intrauterine life. Psychologically it would appear to offer some advantages over the customary practice of swathing the infant and placing him on his back. We have observed that the infants placed on their abdomens cry less than those placed on their backs.

The importance of protecting the infant from contact with bacterial agents is well recognized. This applies particularly to the infant with illnesses which predispose to pneumonia, such as the common cold, influenza, whooping cough, measles, and others. These diseases may combine with bacterial agents to produce the serious complicating diseases such as otitis media, sinusitis, bronchitis, and pneumonia. It is here that chemotherapy may play an important role in prevention and treat-

ment. The identity of the bacterial agents can frequently be determined by means of nasal and pharyngeal smears and cultures. In the predisposing diseases, many of which appear to be due to viruses, smears frequently show epithelial cells only. In certain instances, inclusion bodies occur in great numbers in such cells. When a virulent bacterial agent is prevalent, the smears show contrastingly large numbers of leucocytes and bacteria. It is in patients with such findings that the early use of chemotherapy is most likely to be of prophylactic value. Although no striking results were observed from the use of chemotherapy in infants with primary virus pneumonitis, its value in treating or in preventing the more serious complications caused by bacterial agents can hardly be questioned. Parenteral administration of the sulfonamide drugs is often advisable for temporary use in the very sick infant, but the oral route is preferable when available. The optimal dose varies between 1.0 and 1.5 grains per pounds (0.2 Gm. per kilogram) in a twenty-four-hour period. Blood levels should be used as a guide to determine the maintenance dosage when possible. Levels of 10 mg. per cent have been found to be adequate in the majority of patients with pneumonia.

Immunotherapy in the form of hyperimmune pertussis serum is considered to be of some value in infancy in preventing the pneumonia associated with whooping cough. Likewise, the early use of convalescent measles serum may help to modify the severe complications which are prone to occur in this disease. In our experience, whole adult blood appeared to be of value in modifying the morbidity in infants exposed to epidemic primary virus pneumonitis.[19] Since the mortality in prematurely born infants suffering from this disease is so much higher than it is in normal, full-term infants, it would appear that the latter probably receive some protecting factors from their mothers during the last few weeks of pregnancy. This aspect of the problem is discussed more fully under neonatal immunity later in this communication.

No attempt has been made to detail all of the considerations in the treatment of pneumonia in infancy, as they must necessarily vary with the specific etiology and the needs of the particular patient. It can be said, however, that of all the therapeutic means available oxygen has been found to be the most valuable in the acutely sick infant. It can be administered by nasal catheter, mask, or small tent. Postural drainage has not only proved of value in prevention, but frequently its use in treatment seems to give striking results. Particularly is this evident when thick, tenacious mucus is one of the disturbing factors. Distressing coughs are often promptly relieved by the prone position.

CLASSIFICATION

The following etiologic and pathogenic grouping of the pneumonias of infancy is proposed because it seems to present some advantages over the anatomico-pathologic classification. So commonly is the whole pul-

monary system involved that it means little to speak of bronchopneumonia or interstitial pneumonia. The pneumonias of infancy have been spoken of as "transitional," as they so frequently seem to be. A pathologic consideration would ultimately lead to a diagnosis of "interstitial pneumonia" in most instances. Trask[20] stated, "It is logical to present the pneumonias from a bacteriologic point of view. . . . It is harder to do this in pediatrics because of greater difficulties in establishing a bacteriologic diagnosis. In part, this is due to the usual unavailability of sputum and to the great variety of pneumococci found in children, but it is chiefly because of the variety of the predisposing illnesses and because mixed infections play an outstanding role in the pneumonias of childhood." It must be granted that there will be pneumonias of infancy which we cannot rigidly classify, especially when recovery takes place. Careful and complete history and physical examinations, in addition to bacteriologic, pathologic, and virus studies of the sputum, will aid greatly in properly classifying these diseases. The specific histopathologic differences seen in the thorough examination of necropsy material will often give the final answer to the problem. The following classification is consistent with the Standard Nomenclature of Disease and is presented in the order given in the International List of Causes of Death.

I. Primary bacterial pneumonia
   Pneumococcal, staphylococcal, etc.; tuberculous (first infection type)
II. Primary spirochetal pneumonia
   Syphilitic (pneumonia alba)
III. Primary virus pneumonia
   Primary virus pneumonitis; psittacosis
IV. Primary mycotic pneumonia
   Thrush, blastomycosis, etc.
V. Synergistic or secondary (virus and bacterial) pneumonia
   (Primary diseases include influenza [virus], measles, pertussis, the common cold, etc.)
VI. Secondary virus pneumonia (Goodpasture)
   (Primary diseases include measles, pertussis, and possibly others)
VII. Aspiration pneumonia
   Congenital, amniotic, lipoid, etc.
VIII. Avitaminosis pneumonia
   Vitamin A deficiency associated with chronic fibrous cystic disease
IX. Eosinophilic pneumonia
   (Löffler's syndrome)

SPECIFIC HISTOPATHOLOGY

The predominating pathologic change in most of the pneumonias in infancy is an interstitial mononuclear reaction. Sprunt and co-workers[21] pointed out that an interstitial mononuclear pneumonia is only one

phase of the lung reaction to almost all causes of pulmonary disease. The only partial exception is in the primary and secondary bacterial pneumonias. These pneumonias on occasion will produce a predominantly mononuclear change. Therefore, in order to differentiate the various forms of pneumonia, the specific histopathologic differences will be considered in relation to the etiology and development of each entity. No attempt will be made to describe the pathology of the various types of pneumonia in infancy but merely to point out somewhat specific differences where they exist characteristically, keeping in mind the difficulties incident to the mixed features of many of these types of pulmonary involvement.

Aspiration Pneumonia.—Laughlin[22] in 1925 established the relationship of oily nose drops and lipoid pneumonia in infancy. Pinkerton[23] in 1927 reported six cases of mononuclear pneumonia following the aspiration of lipoids. Fat-laden macrophages and foreign body giant cells set apart the pneumonias resulting from the aspiration of oils (Ikeda[24]). In Holt's textbook it is stated, "In aspiration pneumonia the *Saccharomyces albicans* has been found in the lung."[25] Cultures from the lower trachea and bronchi in a patient recently observed by us revealed the thrush organism and staphylococcus to be present. MacGregor[14] has pointed out the presence of vernix membrane and amniotic debris in the microscopic sections of infants dying of congenital aspiration pneumonia.

Tuberculous Pneumonia.—Both the more benign perifocal tuberculous pneumonias and the more severe caseous pneumonias are seen in infants as a result of primary invasion of the tubercle bacillus into the lung. The specific changes in these lesions are the epitheloid and typical giant cells.

Eosinophilic Pneumonia.—Widespread pulmonary infiltrations of eosinophilic cells coinciding with high blood eosinophilia is diagnostic of Löffler's pneumonia. The blood eosinophiles are larger than normal, with unusually large granules which are fewer in number than normal.[26] Botsztejn[27] reported five cases of pneumonia of young infants. There was a high absolute and relative eosinophilia which accompanied the highest peak of the disease. Pertussiform fits of coughing with severe dyspnea, pleurisy complicating hilar pneumonia, afebrility, and subacute course were the outstanding symptoms. Except for the eosinophilia, these features may all be found in other types of pneumonia in young infants. The coincidence makes a characteristic clinical picture. Von Meyenberg[28] recently reported the only autopsy studies in this disease and found eosinophilic infiltrations in other organs as well as in the lung.

Bacterial Pneumonia.—Primary pneumonia does not ordinarily involve the framework of the lung as does interstitial pneumonia, which experimentally and clinically appears in many instances to be due to the combined action of a virus and a bacterium. The primary and sec-

ondary bacterial pneumonias produce a varied picture, with some characteristics peculiar to each. Staphylococcal pneumonia produces clustered abscesses; influenza bacillus, bronchiolitis, pneumococcus, diffuse and localized consolidations; and hemolytic streptococcus, marked distension of the interstitial lymphatics with focal and diffuse consolidations. Trask[20] stated that the outstanding feature of the autopsy series in children is the prominence of mixed infections. He cited the case of a child who developed a mixed staphylococcal and influenzal pyopneumothorax during a type I pneumococcus pneumonia.

The thickening of the various constituents of the pulmonary system seen in interstitial pneumonia is distinctive. Bronchiolitis and peribronchiolitis, thickening of interlobular and alveolar septa, and infiltrations of lymphocytes and plasma cells are conspicuous. Geisenbauer[29] has recently described the detailed pathologic changes in infants. He stated that the exudate presents a honeycomb appearance, resembles fibrin, but does not take the same stains. The exfoliated alveolar cells frequently contain fatty and lipoid granular inclusions.

Primary Virus Pneumonia.—Primary virus pneumonitis of infants offers a singular opportunity to study the pathology most probably produced by a virus in human lung tissues.[19, 30] Necrosis, ulceration, and proliferation of bronchial epithelium are conspicuous changes. (These same features have been pointed out recently by several authors[31-33] in describing fulminating cases of pneumonia due to influenza virus and *Staphylococcus aureus.*) The exudate is predominantly epithelial and mononuclear; no bacteria and few polymorphonuclear leucocytes are evident. A mononuclear peribronchiolar infiltration adds to the microscopic picture. The specific distinguishing feature in these cases is the presence of characteristic cytoplasmic inclusion bodies in the epithelial cells of the bronchial, bronchiolar, and alveolar tissues. These bodies have definite features, varying in size from 3 to 6 μ, stain acidophilic with the hematoxylin and eosin stain, are frequently surrounded by a clear zone or halo, and sometimes have vacuoles within the substance of the inclusion.

The pathologic characteristics of three cases of sudden death in infants due to pneumonia were previously reported in this JOURNAL by me.[34] A typical mononuclear pneumonia associated with diffuse pulmonary hemorrhage and edema was found in all cases. Additional features were the absence of bacteria and a polymorphonuclear response. The pathologic picture was similar to experimentally produced virus pneumonia in animals. In discussing the nature of virus pathology, Rivers[35] said, "the fact that inflammation occurs in many virus diseases cannot be denied, and, despite the acute nature of some of the diseases, if secondary infections do not intervene, the inflammatory process is usually characterized by an infiltration of mononuclear cells." Sprunt[36] stated that "in virus diseases the mononuclear reaction occurs

in the acute phases of the disease and in others as pneumococcus pneumonia in the stage of resolution."

Secondary Virus Pneumonia.—This disease was first described by Goodpasture and his co-workers[37] in 1939 as a virus infection of the lungs following measles, and in one instance, whooping cough. The unusual pathologic features are the presence of hemorrhage in the lung, isolated or situated about areas of definite inflammatory consolidation, a stringy mucoid exudate, ulcerated lesions in the trachea and scattered areas of necrosis in the mucous glands. "The specific feature of the process was the presence of intranuclear inclusions, which were almost entirely restricted to epithelial cells. The involved cells rapidly underwent necrosis and this was the essential cause of the extensive ulceration."[37]

Syphilitic Pneumonia.—In syphilitic pneumonia the lungs are pale, and they specifically demonstrate extensive hyperplasia of the fibrous elements of the interalveolar tissues. *Treponema pallidum* is found in the large mononuclear cells.

NEONATAL IMMUNITY

The perplexing problem involved in the increased susceptibility of the infant to pneumonia is still unsolved. Woolpert, Detwiler, and coworkers[38, 39] studied the comparative susceptibility of fetal and postnatal guinea pigs to the virus of epidemic influenza. They concluded that there is a gradually increasing resistance to infection with this virus during intrauterine development but with little change thereafter, and that at the time of birth there is a sudden loss of infectibility by routes other than the intranasal. A similar relationship was observed by us[19] in an epidemic of primary virus pneumonitis involving prematurely born and full-term infants. The average age of twelve prematurely born babies at the onset of their disease was thirty-four days, a time interval which tends to eliminate immaturity per se. Ten of the twelve premature infants died, a mortality of 83 per cent. Infants born at term appeared to be much less susceptible in the main, as indicated by the mortality which was only 8 per cent in this group of sixty-two infants. It would appear that resistance to infection with this virus is increased during the last few weeks of pregnancy.

VITAMIN A DEFICIENCY AND PNEUMONIA

In patients with chronic cystic fibrosis of the pancreas, death often results from secondary pneumonia or bronchiectasis. Careful study by Andersen[40] has shown a relatively high incidence, 23 per cent, of severe vitamin A deficiency in these infants. The pathologic change consists of a metaplasia of the epithelial linings of the pulmonary system and other organs associated with xerophthalmia. It seems possible that these lung changes prepare the way for the invasion of secondary pyogenic microorganisms. Blackfan and Wolbach[41] stated that "the early effect

of the deficiency (vitamin A) upon the respiratory mucosa is a satisfactory explanation of the frequency, severity, and persistence of the pneumonias that have been in most instances responsible for death."

THRUSH PNEUMONIA

We have recently observed a small epidemic of what we have chosen to call "thrush pneumonia" in young infants. It is extremely rare for the *Monilia albicans* to produce pneumonia and many series of cases of thrush are reported with no deaths directly attributable to pneumonia. Ludlam and Henderson[42] recently reported on 163 cases of thrush, 20 of whom died of various causes. Ebbs[43] reported a series of 22 cases of fatal thrush esophagitis. Little emphasis is accorded to pneumonia except as a terminal event.

Of eight patients with thrush occurring at the same time in the nursery of a local maternity home, five were transferred to the University of Minnesota Hospital because of outspoken signs of respiratory distress. A diagnosis of pneumonia was confirmed in all infants by x-ray examination. Three additional cases of thrush developed at the University Hospital following admission of these patients. All infants had the typical white patches on the tongue, cheeks, and palate from which *M. albicans* was obtained.

The presence of excessive amounts of mucus in all of the patients was an unusual clinical feature in this series of cases. Most authors call attention to the dry character of the mucous membranes of the mouth and throat in ordinary cases of thrush. Dyspnea was present in seven of the eight infants studied at the University Hospital, and cyanosis was recorded in six. Many of the babies had an elevated white blood count, the average of the highest counts for all patients being 16,275 cells per cubic millimeter. Temperature elevations were recorded in all cases excepting one. Spikes of temperature as high as 101° or 102° F. were characteristic. In two infants, the rectal temperature rose to 104° F. on at least one occasion. The x-ray findings in the lungs showed a diffuse type of central infiltration in seven of the patients.

Six of the eight patients with thrush first observed at the maternity home had evidence of impetigo at the time of the onset of the lesions in the mouth. One of the babies subsequently died, and autopsy revealed a widespread staphylococcic pneumonia with multiple small areas of abscess formation. It seems logical to suggest that the coexistence of the *M. albicans* and the staphylococcus played a concerted role in producing this unusual epidemic of pneumonia. Although the severity of symptoms in these cases was considerably greater than in the ordinary case of thrush, it was only moderate when compared to that of the average case of primary staphylococcic pneumonia. Studies are in progress at present to evaluate further the possible synergistic effects of the *M. albicans* and various strains of staphylococci.

Henderson[44] in a recent (1943) survey of infection in newborn infants during a three-year period found an incidence of thrush infection in approximately 5 per cent of 8,075 infants. The disease occurred in epidemics, causing a mortality of 1.5 per cent. It is interesting to note that the incidence of staphylococcus skin lesions in the entire group of 8,075 newborn infants was 6.8 per cent. He reported that most of the 10-day-old infants had staphylococci in the nose, and 30 per cent of the women admitted in labor had the organism in the anterior nares.

DISCUSSION

The relative importance of air-borne agents as opposed to gravitation or aspiration of bacteria-laden exudates does not indicate a conflict of ideas or facts, as both play a distinct role in the development of pneumonia. In the infant under 2 years of age, the usual primary pneumococcus pneumonias, namely types I, II and VII, are relatively infrequent. This implies that most of the pneumonias may be secondary or complicating infections. Although primary pneumonias may occur, and secondary or complicating pneumonias may follow primary contagious diseases of the upper respiratory tract, there probably exists a large group of pneumonias which are caused by two or more agents acting synergistically or in concert. As mentioned previously, Smillie[4] and others have shown that infants can harbor pathogenic bacteria for long periods of time without symptoms of disease until attacked by an intercurrent epidemic respiratory infection. The previously quiescent pathogens then multiply, frequently producing serious disease. Trask[20] comments that predisposing illnesses are of importance in the pathogenesis of *all* varieties of pneumonia. The concept of synergistic etiology has a direct bearing on prevention and treatment, and, therefore, deserves further discussion.

Shope[45] has established beyond doubt the dual etiology of swine influenza which is caused by the "*bacterium Hemophilus influenzae suis* and swine influenza virus acting in concert." The *H. influenzae suis* is not pathogenic for swine when administered in pure culture by way of the respiratory tract, and the virus component causes a transient mild illness, clinically quite distinct from swine influenza. When administered together, however, a clinically severe illness identical with swine influenza in the field is produced.

McCordock and Muckenfuss[46] produced in animals the complete picture of interstitial pneumonia as seen in many by injecting vaccine virus with a suspension of various types of bacteria. They suggested that interstitial bronchopneumonia results from the combined action of a virus and bacteria. Ordinary primary pneumococcus pneumonia affects the framework of the lung very little, while interstitial pneumonia involves both the bronchiolar walls and the alveolar and interlobular septa. Most cases of interstitial pneumonia occur as a complication of measles, pertussis, or epidemic influenza, according to Holt and Mc-

Intosh.[47] Measles and epidemic influenza are known to be caused by viruses, and pathologic as well as clinical evidence suggests that a virus may play an accessory etiologic role in pertussis in concert with the Bordet-Gengou bacillus.[48] Stokes and Wolman[33] reported pathologic findings in a fulminating respiratory infection which resembled in every respect those found in some of the more severe cases of the 1918 pandemic of influenza. The human influenza virus was found in the lungs in association with *Staph. aureus.* The authors believe that the lesions described during the pandemic of influenza in 1918 are best explained in terms of a synergistic action between a virus and a bacterium. Scadding[31] also observed a "case of fulminating 'influenzal' pneumonia, fatal on the third day, in which both *Staphylococcus aureus* in enormous numbers and the virus were demonstrated." He concludes significantly that the influenza virus can produce severe changes in the lung of man which facilitate invasion by bacteria. In his opinion, the course of the disease depends upon the extent and virulence both of the virus and of bacterial infection; the extraordinary variability of the clinical picture is due to the numerous possible combinations of these factors.[31] Wollenman and Finland[32] likewise reported a combination of both influenza virus and *Staph. aureus* in three fulminating cases of pneumonia which they stated were almost certainly due to infection with both agents. O'Hara[50] commented, "most if not all cases of so-called 'lobar pneumonia' are clinical examples of this sequential or combination attack—by the virus of the common cold and the pneumococcus."

This concept of dual or multiple etiology has particular significance both in the prevention and the management of these cases. The strict isolation of the patient with precursor diseases to prevent further bacterial contact is readily appreciated. The early recognition of all possible agents involved, particularly the bacteria, will greatly influence our choice of chemotherapeutic agents and the early use of them when indicated. Studies now in progress in our laboratory on the value of pharyngeal smears in diagnosis may prove to be of some assistance. In a recent epidemic of influenza caused by type A virus, smears of the pharyngeal exudate revealed large numbers of epithelial cells and a scarcity of leucocytes and bacteria in the uncomplicated cases. When pathogenic bacteria occur in large numbers, the character of exudate is quite different, numerous leucocytes being added to the other elements present. This same modification was noted in the pharyngeal smears taken from infants with another form of virus pneumonitis when the latter was complicated by bacterial invasion. In this condition, cytoplasmic inclusion bodies were found in many of the epithelial cells. Frisch and associates[51] have been able to differentiate the mild, moderate, and critically ill patients with pneumonia by means of pneumococcus counts on the admission sputum. If the count did not exceed ten pneumococci per field, the case was considered as mild, whereas a count

of from thirty-six to fifty indicated a severe case and therapy was determined accordingly.

The value of early cultures should not be overlooked. Rickard and associates[52] have recently been able to isolate and identify influenza virus type A from untreated, unfiltered throat washings by direct intra-allantoic inoculation of the developing chick embryo. The Hirst red cell agglutination-inhibition test was used for identification. This relatively simple procedure should serve to check the present confusing and too-often-made diagnosis of "flu." The significance of influenza virus infections cannot be overemphasized as a cause of respiratory disease which may produce serious fulminating pneumonia when associated or combined with pathogenic bacteria. Statistics of the pandemic during World War I showed that approximately 20 per cent of influenza patients developed pneumonia of bacterial etiology.[1] In a recent study[53] of a proved epidemic of influenza type A in infants and children at the University of Minnesota Hospitals, no patients with pneumonia were observed. Twenty-four cases were included in the study. Acute pharyngitis and high biphasic fever, occasionally reaching 105° F., were characteristic. The immediate complications were mild. Two patients developed otitis media, and one patient had acute bronchitis. The serologic responses in all of the infants were as striking and definite as those noted in older individuals.

SUMMARY

Recent advances in our knowledge regarding the pathogenesis of pneumonia in infancy have been recounted. It is apparent from the data assembled that the aspiration or gravitation of bacteria-laden exudate plays a more significant role in the inception of pneumonia than does the inhalation of bacteria-containing droplets from the atmosphere. Additional important contributory factors are: (1) immaturity of the lungs, both anatomic and physiologic; (2) lack of neonatal immunity; (3) vitamin A deficiency; and (4) conditions associated with birth, such as asphyxia. The latter greatly increases the incidence of congenital aspiration pneumonia.

Air-borne infections such as the common cold and epidemic influenza are predisposing illnesses which greatly increase the activity of the potential pathogens frequently resident in the upper respiratory tract. Evidence is presented to support this conception regarding the dual or multiple etiology of many of the pneumonias of infancy. Air-borne agents and bacteria-laden exudates play a combined role in their development.

An unusual epidemic of "thrush pneumonia" is described, in which the synergistic action of the *M. albicans* and a strain of staphylococcus were considered as having a possible causative relationship.

The specific histopathologic changes characterizing the various types of pneumonia in infancy are described, and a system of classification based on etiology and pathogenesis is offered.

Recognition of the many etiologic factors in the pneumonias of infancy is significant for their prevention or management. In so far as the prone position helps to prevent the gravitation or aspiration of bacteria-laden exudate into the lungs, compensating for the immature development of the mechanisms of elimination, such as cough and ciliary action, it may be regarded as a means of preventing pneumonia in infants. By its habitual use, the hazard of "sudden death" or "crib death" of pneumonic origin would probably be eliminated. The strict isolation of patients with predisposing illnesses is another factor to be taken into account to avoid further infection by pathogenic bacteria. The prone position offers an effective means of preventing or treating the type of cough which is related to obstructing exudate in the upper respiratory passages.

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EXPERIENCE WITH SULFAPYRAZINE IN CHILDREN

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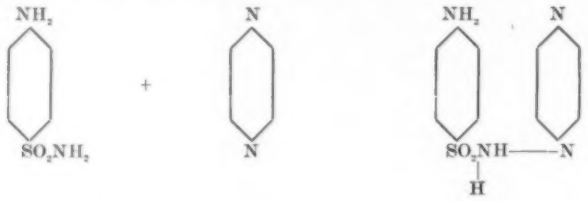
DURHAM, N. C.

SINCE the advent of sulfanilamide many similar drugs have been synthesized in an attempt to find one of extremely high bacteriostatic activity and of low toxicity. Among the latest of these many compounds is 2-sulfanilamido-pyrazine, or sulfapyrazine.[1]



Sulfanilamide pyrazine Sulfapyrazine

Sulfapyrazine is a crystalline white powder only slightly soluble in water (about 5 mg. per cent). The sodium salt, however, is highly soluble. Little of the drug is acetylated by the body. Experimental studies with sulfapyrazine in animals have shown it to be of very low toxicity,[2, 3] and its effectiveness in adults[2] has already been reported. For this reason it was decided to study its therapeutic effectiveness and toxicity in children.

One hundred and nineteen unselected pediatric hospital patients were studied from July 1, 1943, to Feb. 28, 1944. Those with only moderate infections were treated by the oral route. Children with more severe infections were given the drug intravenously or subcutaneously and then later carried on by oral administration. Blood levels were determined at hourly and daily intervals.

Oral Administration.—Blood levels were obtained on all patients at 24-, 72-, and 96-hour intervals. Infants received 1 grain (0.064 Gm.) per pound of body weight per twenty-four hours, one-half being given as an initial dose and the total dosage being divided into six daily doses, making the dosage 1½ grains per pound in the first twenty-four hours. Children over 6 years of age received 2 Gm. sulfapyrazine initially and 0.5 Gm. every four hours. As shown in Fig. 1 the maximum drug concentration is reached in four hours, indicating that sulfapyrazine should be administered at four-hour intervals. Other observers feel that due to the slow excretion of sulfapyrazine the difference between the 4- and 6-hour levels is not great enough to alter the bacteriostatic activity of the drug.[4]

From the Department of Pediatrics, Duke University School of Medicine, and Duke Hospital. The sulfapyrazine was furnished through the courtesy of Mead Johnson and Company.

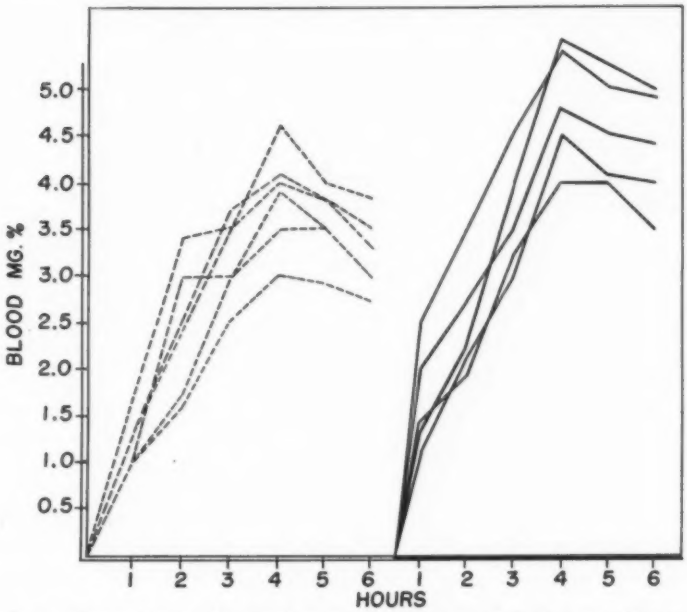


Fig. 1.—Hourly blood levels to show peak of blood concentration of sulfapyrazine on a single oral dose of 1 grain per pound.----------under 2 years; ———— over 2 years.

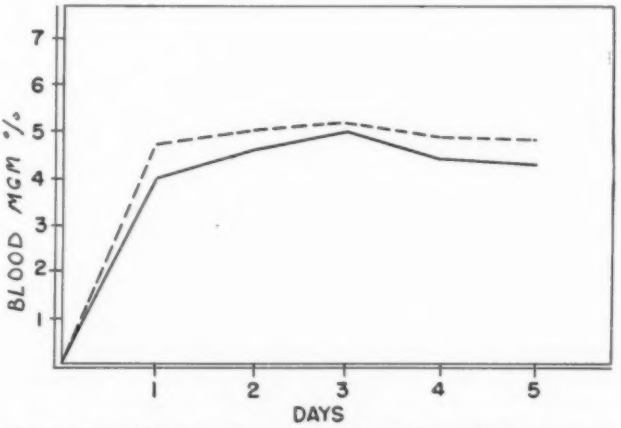


Fig. 2.—Comparison of blood levels on single and double oral dosage. ———— 1 grain per pound; ----------2 grains per pound.

It was observed early in the course of this study that the 24-hour blood level of all patients regardless of age was lower than that seen with the other sulfonamides. In an effort to see if a higher blood level could be obtained by oral administration the blood levels of twelve patients who received the dosage described were compared with those

of twelve patients who were given double these amounts. As shown in Fig. 2 the difference in dosage was of little significance. The drug is apparently absorbed rather slowly from the gastrointestinal tract and increasing the amount of available drug does not speed up the rate of absorption. Thus a comparatively low blood level is obtained from either dose, but this level is therapeutically as effectively as the higher level obtained with other sulfonamides.

Intravenous Administration.—Twenty-one patients were considered sufficiently ill to warrant 1 per cent sodium sulfapyrazine intravenously in a dosage of 1½ grains (0.096 Gm.) per pound of body weight per twenty-four hours. Sulfapyrazine was then given orally. The intravenous administration gave a high initial level (Fig. 3), which was difficult to maintain unless the injection was repeated at frequent intervals, an impractical procedure in infants and children. Also, the high levels which are produced immediately after an intravenous injection increase the chance of renal damage. Of these twenty-one patients, one had gross hematuria and one, microscopic hematuria for one day only.

Subcutaneous Administration.—Many patients with moderately severe infections who were unable to retain the drug by mouth were treated by the subcutaneous injection of a 0.5 per cent solution of sodium sulfapyrazine in normal saline, the dosage being ½ grain (0.032 Gm.) per pound of body weight every eight hours for from twenty-four to forty-eight hours. Sulfapyrazine was then given orally. In this manner a quite high blood level was maintained (Fig. 4), and the fluid requirements of the patients were satisfied. The apparent drop of the blood level is due to the patients being transferred to oral sulfapyrazine. For acutely ill children in whom an immediate high level is desired the subcutaneous route probably is better than intravenous administration.

Sulfapyrazine in the Spinal Fluid.—Sulfapyrazine diffuses into the spinal fluid in about the same degree as the other sulfonamides, that is, reaching a level of from about 50 to 60 per cent of the blood level. Nine patients had spinal fluid determinations, five of them received initial intravenous sulfapyrazine and had spinal fluid and blood determinations done at twelve hours and frequent intervals thereafter (Fig. 5). The other four were given only oral sulfapyrazine with spinal fluid levels run at twenty-four hours and repeated as seen in Fig. 6.

Evaluation of Effectiveness of Sulfapyrazine.—From July 1, 1943, to Feb. 28, 1944, 119 unselected pediatric patients were treated with sulfapyrazine. The diseases treated were the usual ones seen in a children's hospital, Table I. The results were similar to those usually obtained with sulfadiazine.

Toxicity of Sulfapyrazine.—The patients treated were watched closely for the toxic reactions known to occur with the other sulfonamides and for any other untoward clinical or laboratory reactions.

1. *Fever:* In only one patient was fever presumed to be due to sulfapyrazine, but this may not have been true, as the child was given

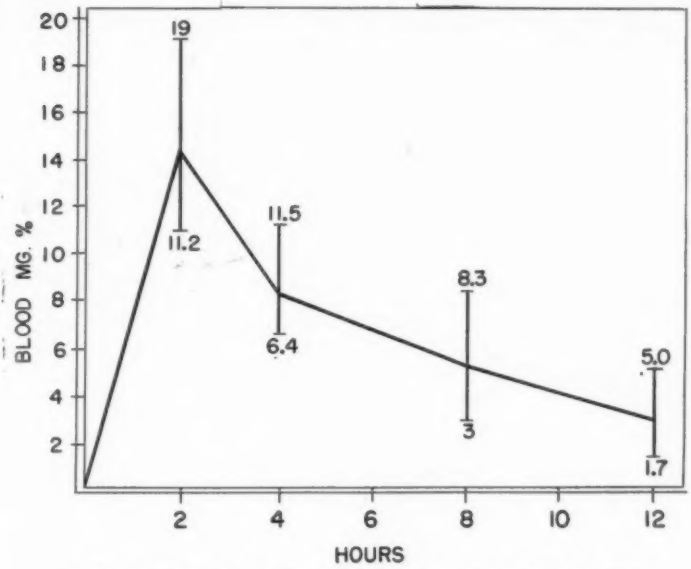


Fig. 3.—Average level by intravenous route showing range of levels.

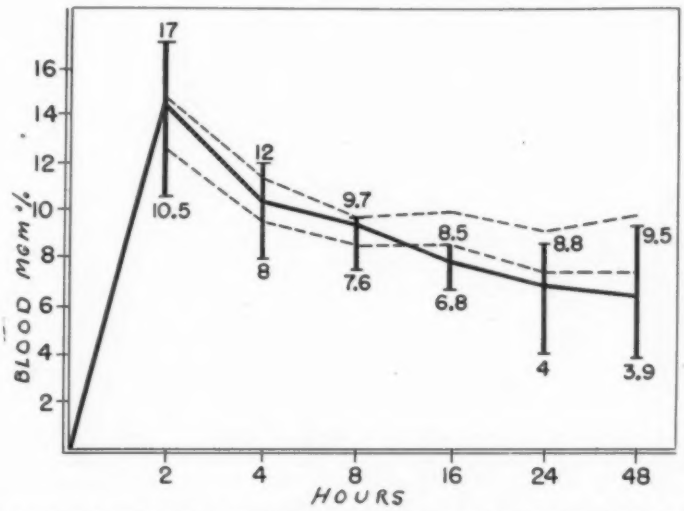


Fig. 4.—Average blood level obtained by subcutaneous administration showing range of levels. ————————average; - - - - - - - - - - - - - - - - 2 typical cases.

the drug for twenty-four hours before discharge and there was no elevation of temperature.

2. *Nausea and Vomiting:* In no patient was there any nausea or vomiting attributable to sulfapyrazine.

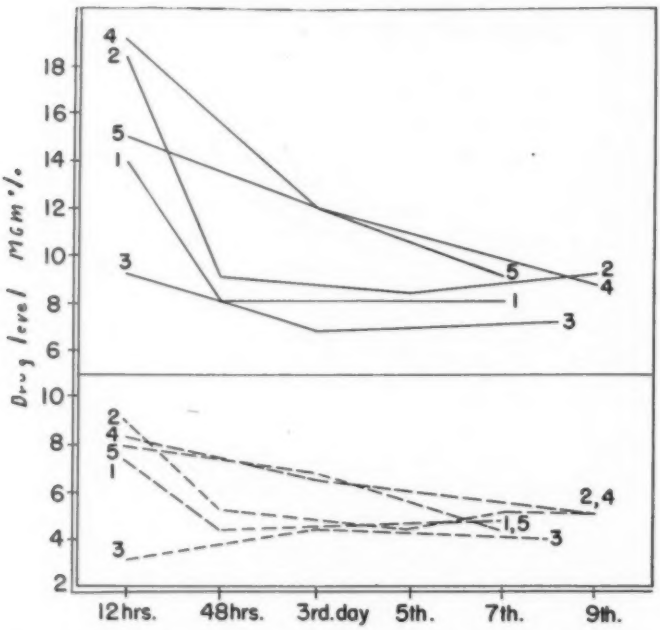


Fig. 5.—Blood and spinal fluid drug levels with initial intravenous drug.———— blood levels; ----------spinal fluid levels.

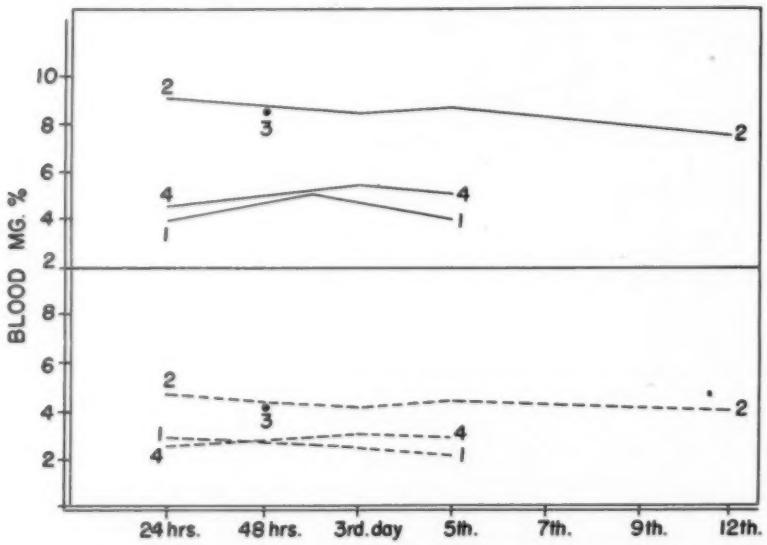


Fig. 6.—Blood and spinal fluid drug levels with oral drug only————————blood levels; ----------spinal fluid levels.

TABLE I

DISEASE	PATIENTS (NO.)	DAYS ON DRUG (AVERAGE NO.)	DAYS FOR TEMPERATURE TO REACH 37°	AVERAGE TOTAL DOSE OF DRUG (GM.)	RESULTS	REMARKS
Meningococcus meningitis	3	10	3.7	31.1	All recovered	No sequellae
Pneumococcus meningitis	3	7.9	5.5	32.6	1 died 2 recovered	1 patient died 7 hr. after administration; one of the recovered patients also received penicillin
Influenzal meningitis	2	22	7.5	20.7	1 died 1 recovered	Also received type B anti-influenzal serum; fatal case (no serum)
Bronchopneumonia	16	5	2.1	8.9	All recovered	Culture revealed *Staphylococcus aureus* in 11 cases and 5 cases of beta hemolytic streptococcus
Lobar pneumonia	6	6.4	2.2	23.3	All recovered	Type 1 in 2 cases; 4 cases not typed
Otitis media	7	5.6	2.2	9.2	All recovered	All *Staph. aureus*
Nonspecific upper respiratory infection	18	5.6	2.4	11.4	2 tracheobronchitis expired	Cases included tonsillitis, pharyngitis, and tracheobronchitis
Specific diarrhea[6]	6	6	3	10.5	All recovered	2 Hiss Russell Y; 2 Flexner; 1 salmonella, 1 para A
Parenteral diarrhea[6]	23	6.4	3	4.8	All recovered	Two patients did not respond and had to be placed on another sulfonamide
Acute hemorrhagic nephritis	4	7.5	2.2	20	All recovered	These patients had infection of nose and throat; levels were no higher; urine cleared while on treatment
Staphylococcus septicemia	2	10	No improvement	41	2 died	One patient also received penicillin; the other received all of the sulfonamides
Pneumococcus septicemia	3	6	2.1	19	All recovered	Chronic nephritis in these patients; blood cultures sterile on third day in 2 patients, on fourth day in third; no change in primary condition
Subacute bacterial endocarditis	3	18	All received fever therapy	174	No change	One patient had blood stream sterilized for seven weeks; 2 patients have since expired
Miscellaneous cases	23	6.5	4.2	15	1 diphtheria and 1 postoperative meningomyelocyle expired	Other cases treated were diphtheria 1, typhoid 2, pneumonia 3, impetigo 3, ulcerative colitis 1, pertussis 3, hemorrhagic chickenpox 1, prophylaxis preoperatively in tonsillectomy and adenodectomy, 7

3. *Rash:* No definite or even suggestive cutaneous manifestations were seen in any patient.

4. *Renal Complications:* Of all the toxic reactions to the sulfonamides, renal irritation is the most serious. They should be divided into gross or microscopic hematuria. Gross hematuria is a warning to stop the drug immediately. In these 119 patients only one case of gross hematuria was observed and it followed the intravenous administration of sodium sulfapyrazine when the blood level was 21 mg. per cent. The patient was receiving soda bicarbonate, but the hematuria occurred while the urine was still acid. In this one patient, the drug was stopped, fluids were forced, sodium bicarbonate was continued, and the urine cleared in forty-eight hours. The patient was then given sulfapyrazine orally and hematuria did not recur. The nitrogen retention was not increased and there was no oliguria. Nine patients had transitory microscopic hematuria. One of these children had red cells for two days and the remaining eight patients had red cells on only one occasion. In none of these nine patients was there any elevation of the nonprotein nitrogen, and the drug was continued in each case.

5. *Leucopenia:* A white blood cell count was done every other day in all patients receiving sulfapyrazine and not in a single incidence was it necessary to discontinue the drug because of a precipitous drop in the white blood cell count.

6. *Anemia:* The hemoglobin and red blood cell count were followed in conjunction with the white blood cell count, but there was not a single case of anemia as the result of sulfapyrazine.

7. *Other Reactions:* There were none which could be classified as toxic effects of sulfapyrazine.

8. *Sensitivity:* One patient received sulfapyrazine on five different occasions and four others on two to four occasions without developing any evidence of sensitivity.

Discussion: As stated earlier in this communication it was found that with sulfapyrazine the blood levels obtained were much lower than those obtained with sulfadiazine. This same observation had been made previously by Hamburger and associates[2] and later by Barnett and coworkers.[4] Because of these lower levels a double oral dosage was used in an effort to obtain a higher and presumably more effective blood concentration. Doubling the dosage increased the blood level by only 0.5 mg. per cent, regardless of age. These lower blood levels were, however, as effective as higher levels when other sulfonamides were administered.

Immediate high blood levels can be obtained by intravenous administration of sodium sulfapyrazine, but in infants this is the most difficult route of administration. As the only case of gross hematuria was seen during the peak of blood concentration following intravenous administration and high levels are not necessary, it seems best to avoid this method of administration. To offset this the subcutaneous route

is the most effective way of establishing an adequate blood level in infants. A stable level can be maintained and the patients' fluid requirements can be met.

Sulfapyrazine reaches an effective level in the spinal fluid at about the same rate as the other sulfonamides. An adequate level is reached in twelve hours and is present in a concentration of between 50 to 60 per cent of the blood level.

This series did not allow for a statistical comparison between sulfapyrazine and the other sulfonamides, but from the 119 cases it is apparent that sulfapyrazine is as therapeutically effective as the other drugs, that high blood levels are not necessary, and while the series is small the scarcity of toxic reactions makes it appear that in sulfapyrazine we have a drug of high potency and extremely low toxicity. It is an excellent drug for all types of infections in infants and children.

CONCLUSIONS

1. Sulfapyrazine administered orally in a dosage of 1 grain (0.064 Gm.) per pound of body weight results in low blood levels which are therapeutically effective.

2. An increased dosage does not effectively raise the blood concentration.

3. Subcutaneous administration was effective.

4. Spinal fluid concentrations were found to equal from 50 to 60 per cent of the blood level.

5. The only toxic reactions found in 119 infants and children treated by sulfapyrazine were one case of gross hematuria after intravenous therapy (0.84 per cent) and nine instances of transient microscopic hematuria (7.5 per cent).

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ROENTGEN STUDIES OF THE HEART IN ASTHMATIC CHILDREN

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A REVIEW of the literature would indicate that bronchial asthma is a contributing factor in the production of heart disease. These studies have all been made on adults where other disease processes are often concomitant. In order to study this problem we have selected a number of children all of whom have had bronchial asthma for a number of years. (Table I.)

Inasmuch as the demonstration of cardiac enlargement is accepted as one of the pathognomonic signs of heart disease we subjected these children to physical examination and x-ray study in order to determine the presence or absence of cardiac hypertrophy. We are cognizant of sources of error in this approach to the problem. An individual with a high diaphragm might clinically present an enlarged heart; nevertheless this organ would be perfectly normal. On the other hand, ptotic individuals with dropped hearts could have considerable cardiac enlargement and the heart size would appear within normal limits. Since the asthmatic child rarely comes to autopsy, these methods of approach seem the only applicable ones. The accompanying reproductions of roentgenograms represent typical configurations of the heart and great vessels in these asthmatic children. (Figs. 1, 2, 3, 4.)

The standard methods of estimating heart size from roentgen examination were employed. After a preliminary fluoroscopy by Dr. J. N. Ané, two meter plates employing standard technique were taken of all the subjects. Table II presents measurements of the transverse diameter of the great vessels, the longitudinal diameter of the heart, the broad diameter, and the results of the fluoroscopic examination. It will be observed that these data are all within normal limits. Table III represents the results obtained by the use of prediction formulas for the transverse diameter of the heart using height and weight ([a] $T = 0.0637W + 7.5$; [b] $T = 0.00490H + 0.05694W + 7.1$). In parallel columns the actual transverse diameters of these hearts are recorded for comparison. It will be seen in column 3 which represents the algebraic difference of the actual and the predicted transverse diameters that there is a very close correlation using both formulas. With but three exceptions, the actual transverse diameter is less than the predicted diameter, and in these the difference is minimal.

From the Department of Medicine, School of Medicine, Tulane University and Charity Hospital of Louisiana.

TABLE I

GENERAL INFORMATION RELEVANT TO ASTHMATIC CHILDREN

CASE	SEX	COLOR	AGE IN YR.	DURATION OF ASTHMA IN YR.	CARDIAC SYMPTOMS	CARDIAC SIGNS
L. L.	M	W	11	8	0	0
J. D.	M	W	7	3	0	0
W. F.	M	W	7	4	0	0
B. M.	M	W	7	4	0	0
S. L.	M	C	14	6	0	0
D. B.	M	W	14	7	0	0
C. W.	F	W	13	3	0	0
C. R.	M	W	11	9	0	0
J. M.	M	W	5	3	0	0
T. K.	M	W	5	4	0	0
R. D.	M	W	7	1	0	0
M. C.	M	W	10	2	0	0

TABLE II

CARDIAC DATA DERIVED FROM THE X-RAY

CASE	TRANSVERSE DIAMETER OF GREAT VESSELS	LONGITUDINAL DIAMETER OF HEART	BROAD DIAMETER OF HEART	FLUOROSCOPY
L. L.	4.0	10.5	8.2	Normal
J. D.	4.6	10.3	9.1	Normal
W. F.	4.4	9.0	7.9	Normal
B. M.	4.2	10.0	7.2	Normal
S. L.	4.9	12.9	10.4	Normal
D. B.	5.6	12.3	9.5	Normal
C. W.	4.9	13.0	10.0	Normal
C. R.	5.2	12.1	10.2	Normal
J. M.	4.7	9.7	8.1	Normal
T. K.	4.1	9.6	7.4	Normal
R. D.	4.0	9.9	8.7	Normal
M. C.	4.9	10.7	8.6	Normal
H. R.	4.0	8.1	8.4	Normal

TABLE III

PREDICTION FORMULAS FOR TRANSVERSE DIAMETER OF HEART USING HEIGHT AND WEIGHT

(a) $T = 0.0637W + 7.5$				(b) $T = 0.00490H + 0.0569W + 7.1$			
CASE	T_P	T_A	$T_A < T_P$ BY CM.	CASE	T_P	T_A	$T_A < T_P$ BY CM.
L. L.	9.4	8.4	1.0	L. L.	9.5	8.4	1.1
J. D.	9.3	9.5	-0.2	J. D.	9.3	9.5	-0.2
W. F.	8.8	8.2	0.6	W. F.	8.9	8.2	0.7
B. M.	8.9	8.9	0.0	B. M.	9.0	8.9	0.1
S. L.	10.6	11.1	-0.5	S. L.	10.6	11.1	-0.5
D. B.	10.9	10.0	0.9	D. B.	11.0	10.0	1.0
C. W.	10.5	9.8	0.7	C. W.	10.5	9.8	0.7
C. R.	10.8	10.5	0.3	C. R.	10.2	10.5	0.2
J. M.	8.8	9.2	-0.4	J. M.	8.8	9.2	-0.4
T. K.	8.8	8.8	0.0	T. K.	8.8	8.8	0.0
R. D.	9.2	8.6	0.6	R. D.	9.2	8.6	0.6
M. C.	9.6	9.5	0.1	M. C.	9.6	9.5	0.1

Fig. 1.—L. L., 11-year-old white male; duration of asthma eight years; physical examination negative; etiologic antigens: pyrethrum, ragweed, house dust.

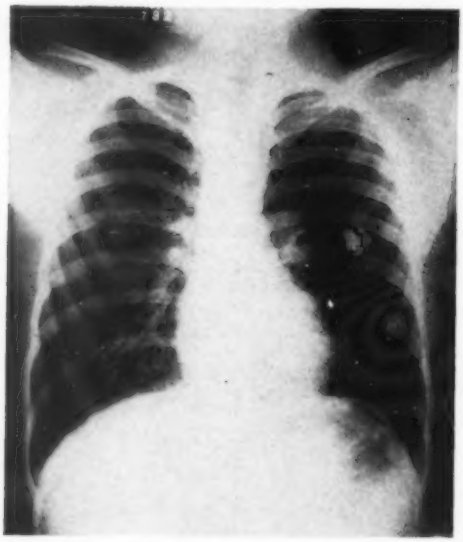

Fig. 2.—M. C., 10-year-old white male; duration of asthma two years; physical examination negative; etiologic antigens: feathers, dog hair.

Fig. 3.—W. F., 7-year-old white male; duration of asthma four years; physical examination negative; etiologic antigens: wheat, house dust.

Fig. 4.—D. B., 14-year-old white male; duration of asthma seven years; physical examination negative; etiologic antigens: eggs, kapok.

TABLE IV

PREDICTION FORMULAS FOR TRANSVERSE DIAMETER OF HEART USING CARDIOTHORACIC RATIO

CASE	INTERNAL DIAMETER OF CHEST T_I	TRANSVERSE DIAMETER OF HEART T_A	$2T_A < I$ BY CM.
L. L.	21.5	8.4	4.7
J. D.	23.8	9.2	4.8
W. F.	19.5	8.2	3.1
B. M.	18.8	8.9	1.0
S. L.	25.3	11.1	3.1
D. B.	27.3	10.0	7.3
C. W.	25.0	9.8	5.4
C. R.	26.0	10.5	5.1
J. M.	19.9	9.2	1.5
T. K.	19.0	8.9	1.8
R. D.	21.1	8.6	3.9
M. C.	25.0	9.5	6.0
H. R.	18.9	8.0	2.9

Table IV indicates the distribution of the cardiothoracic ratio of Danzer.[1] Here again, in every instance, the findings are well within the limits of the customarily accepted formula $2T < I$. Table V illustrates the findings obtained by applying the data to the Eyster-Hodges

TABLE V

COMPARISON BETWEEN CARDIAC AREA AS DETERMINED BY THE EYSTER-HODGES NOMOGRAM AND BY COMPUTATION

CASE	AREA DETERMINED BY EYSTER-HODGES NOMOGRAM	AREA DETERMINED BY FORMULA $A = \frac{LB\pi}{4}$	ALGEBRAIC DIFFERENCE IN SQUARE CENTIMETERS
L. L.	71.0	67.6	+ 3.4
J. D.	67.0	73.6	- 6.6
W. F.	58.0	55.8	+ 2.2
B. M.	59.0	55.3	+ 3.7
S. L.	93.0	105.0	-12.0
D. B.	101.2	91.7	+ 9.5
C. W.	93.0	102.1	- 9.1
C. R.	98.0	93.0	+ 5.0
J. M.	66.5	61.0	+ 5.5
T. K.	54.0	40.09	+13.91
R. D.	67.0	67.8	- 0.8
M. C.	75.8	72.2	+ 3.6
H. R.	51.0	50.0	+ 1.0

nomogram[2] of cardiac area for children and the area of the cardiac silhouette which was obtained by using the formula $\frac{LB\ \pi}{4}$. For the most part, there was a close agreement in the figures obtained by these two methods.

DISCUSSION

We are fully aware that there is no absolutely certain method of determining heart size ante mortem. We feel, however, that by applying all of the available methods, that is, physical examination, fluoroscopy, and teleoroentgenograms, essentially correct estimations will

be obtained. The statement of Comeau and White[3] that the cardiothoracic ratio is not reliable and should be discarded, will probably be accepted generally. In employing this and all the other methods one must bear in mind the patient's habitus and the position of the heart in the thorax.

The estimation of the cardiac area is a particularly difficult procedure because the outline of the superior and inferior aspects of the cardiac silhouette is obscured by the great vessels, in the first place, and by the shadow of the diaphragm, in the second. It would depend too much on individual variation in where one shadow ends and the other begins. Fluoroscopy by an experienced radiologist and prediction tables remain the best approach to this problem.

CONCLUSION

In conclusion, therefore, we feel from the data submitted that uncomplicated bronchial asthma is not a factor in heart disease. This does not militate against the production of heart disease subsequent to pulmonary fibrosis, emphysema, bronchiectasis, and other pulmonary complications seen in the chronic asthmatic state.

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INTRAVENOUS FEEDING OF A COMPLETE DIET IN A CHILD

Report of a Case

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NOURISHMENT by vein has been a common pediatric procedure for many years. We believe that the case being presented, however, is unique in that the entire water and caloric requirements were given by vein, with fat, carbohydrate, amino acids, and water in the proportions usually recommended for infant diets.

Parenteral glucose and saline therapy has been used effectively and is familiar to every physician. Recently, amino acids[1] have been used intravenously in a great variety of conditions, including low protein edema, diarrhea, nephrosis, and in various states in which the protein intake is inadequate, notably with suspension of oral feedings during surgical procedures, etc. However, glucose and saline solutions plus amino acids are not a complete answer to the problem of intravenous feeding, because of the difficulty of supplying adequate calories without making the volume of the infusion excessive. The administration of fat is a means of overcoming this difficulty. Although the intravenous injection of fat is not a generally familiar or available procedure, it has, nevertheless, been shown to be practicable and has been used by a number of workers. Holt, Tidwell, and Scott[2] have reviewed the experiences of investigators with parenteral fat in human beings and in experimental animals and stated several theoretical therapeutic values of fats. After describing the development of a practical preparation of emulsified fat safe for intravenous use, they discussed its administration in sixteen children and the possible limitations of its use. Studies of respiratory quotients by Gordon and Levine[3] gave indications that fat given by vein can be oxidized.

The only report in which carbohydrate, amino acids, and fat were given together is that of Clark and Brunschwig.[4] The quantities used did not meet the standard caloric requirements, although the patient maintained his nutritional state and remained in positive nitrogen balance.

The following case report describes the intravenous administration in a child of all three major food constituents in adequate quantities and suitable proportions.

From the Harriet Lane Home, Johns Hopkins Hospital, and the Department of Pediatrics, Johns Hopkins University.

CASE REPORT

D. R. (HLH No. A29888).—The patient was a 5-month-old white infant who had been chronically constipated all his life and had failed to gain well. The birth weight was 4 kg. From the beginning he took feedings poorly and after ten days of breast feeding was given various combinations of evaporated milk, water, and sugar, with no permanent improvement. He was given adequate supplements of ascorbic acid and pereomorph oil. On several occasions he had severe bouts of vomiting associated with fecal impaction, but evacuation of the rectum and colon relieved the vomiting. Nearly every day after the tenth day of life he was given enemas of 250 to 500 c.c. of fluid. Mild laxatives were tried as alternatives to the enemas but with such little success that at times impacted feces had to be removed manually. Although he had gained several pounds by 3½ months of age, during the month and a half previous to admission his course was in general downhill, with loss of weight, poor eating, and increased difficulty in evacuating the colon.

On admission at 5 months of age the patient weighed 4,150 Gm., just 150 Gm. more than at birth. He was dehydrated and extremely emaciated. There was a mild upper respiratory infection. The heart and lungs were normal. The abdomen was distended, soft, and doughy, but the entire colon could be well outlined by palpation and contained large quantities of stool and flatus. The stools were pasty yellow and not foul smelling. X-ray examination showed marked dilatation of the colon, sigmoid, and rectum. The diagnosis was Hirschsprung's disease associated with an upper respiratory infection, vomiting, and extreme malnutrition.

The child was given a formula of Biolac, but it was taken rather poorly. The colon readily became distended with large quantities of feces which were difficult to expel. Often the rectum had to be partially evacuated digitally before enemas were effectual. A course of atropine therapy was given without improvement. He continued to do poorly, exhibited frequent episodes of vomiting, and finally became so emaciated that the fat pads in his cheeks were absorbed. Subcutaneous and intravenous infusions of glucose and amino acids were not sufficient to maintain his nutrition, although they did correct an episode of low protein edema. The patient eventually presented the most extreme picture of marasmus. His face showed the typical wrinkled appearance of an old man. There was almost complete lack of subcutaneous fat everywhere. The impression of all observers was that he would not survive more than a day or two at the most. At this time it was decided to withhold all feedings by mouth, to give his gastrointestinal tract a complete rest, and to provide his nutritive requirements entirely by vein.

The preparations available for intravenous administration were 50 per cent glucose, a 10 per cent solution of amino acids (Amigen), and a 10 per cent emulsion of fat. The fat emulsion consisted of olive oil and lecithin in a 2:1 ratio, suspended in water, the total lipid concentration being 10 per cent. This material was passed through a dairy homogenizer and was subsequently given sixty minutes of supersonic irradiation to cause further dispersion of the fat particles, as described by Myers and Blumberg.[5] The fat globules did not exceed 1 to 2 μ in diameter.

The quantities and proportions of glucose, amino acids, and fat to be given by vein were determined in the following manner. On the basis

of 130 calories per kilogram per day, the daily requirement of an infant weighing 4 kilograms was calculated as 520 calories. The parenteral feeding was designed to provide 58 per cent of the calories (300 calories) from carbohydrate, 12 per cent (60 calories) from amino acids, and 30 per cent (160 calories) from fat. This required the daily administration of 150 c.c. of 50 per cent glucose, 150 c.c. of 10 per cent amino acids, and 180 c.c. of 10 per cent fat emulsion. An additional 120 c.c. of normal saline solution was given, making a total fluid intake of 600 c.c. per day.

To administer these preparations a continuous intravenous drip apparatus was used. A 20 gauge needle with a stylet was tied in place in the left saphenous vein just anterior to the medial malleolus in the left ankle. The remainder of the apparatus consisted of an open-top, graduated cylinder, connected by rubber tubing to a Murphy drip and from there to a metal attachment which could be inserted into the needle. The solutions, in the quantities determined above, were introduced into the apparatus on the following schedule: 12 midnight, 60 c.c. of 10 per cent fat emulsion; 3 A.M., a mixture of 50 c.c. of 50 per cent glucose, 50 c.c. of 10 per cent amino acids, and 30 c.c. of normal saline solution. At 8 A.M. and at 4 P.M. these solutions were repeated in the same order. The rate of flow was adjusted so that the administration of one solution was finished at about the time the next one was due, but if any solution ran in completely before the time was up, the apparatus was disconnected and the stylet used to close the needle. Later, the solutions were permitted to run in faster, so that the drip was intentionally interrupted for periods as long as four hours. The use of the stylet permitted the interruption of the infusion at any time, so that the baby could be moved, turned, or weighed, and the apparatus cleaned and sterilized. The chief purpose in introducing the solutions separately, instead of mixing them all together, was to avoid having the fat stand for any length of time in contact with saline, since solutions of electrolytes neutralize the charge of fat emulsions and cause, in time, some coalescence of the fat particles into larger aggregates.

The intravenous feeding was maintained for a period of five days, during which time nothing was given by mouth. On two occasions small transfusions of blood were given through the apparatus. On the third day the needle was changed to the vein in the right leg. The only untoward reaction of the procedure was a moderate degree of phlebitis of the saphenous veins which responded promptly to compressing.

Toward the end of the period the baby was obviously more vigorous. The fat pads of the cheeks had returned, the ribs were less prominent, and the general nutritional state was much improved. His former expression of dire misery was gone. The response to his environment and to people was more nearly that of a normal child. At the termination of the intravenous feeding, he was given a formula of Olac in gradually increasing quantities. Evacuation of the colon was regulated successfully by prostigmine and enemas. He did unusually well, gained weight rapidly, and was discharged seventeen weeks after admission, having gained 2,860 Gm.

SUMMARY

A 5-month-old white infant with Hirschsprung's disease, complicated by a digestive upset and upper respiratory infection, developed a most

extreme picture of marasmus which gave every indication of an impending fatal termination. The baby was given a complete intravenous feeding for five days with fats, carbohydrate, and amino acids in proportions and quantities recommended in a normal infant's diet. There was a prompt dramatic improvement in the nutrition, permitting eventual successful treatment of the Hirschsprung's disease with prostigmine. We believe that this is the first case on record of complete feeding by vein alone for a significant period of time. The success in this child suggests strongly that total feedings by vein can be a practical and lifesaving procedure, especially applicable to children who are marasmic, or are for any reason unable to handle an adequate diet by mouth, or in whom it is desirable to withhold oral feedings for therapeutic purposes.

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ACCIDENTAL MECHANICAL SUFFOCATION IN INFANTS

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EACH year, for the past decade, an increasing number of children in the United States have been dying from accidental mechanical suffocation (Table I). It is of particular concern that of these fatalities from 70 to 80 per cent have occurred consistently in infants under 1 year of age. The literature has, however, paid but scant attention to accidental mechanical suffocation as a cause of death in early infancy.[1] The problem has remained, furthermore, a sadly neglected field in preventive medicine.

For example, consider the situation in the City of New York (Table II) where the annual deaths from accidental mechanical suffocation have exceeded those from measles, scarlet fever, and diphtheria combined and have equaled those from whooping cough.[2] Strikingly enough, here, too, it will be noted that about 80 per cent of the fatalities from accidental smothering involved infants under 1 year of age.

The problem, therefore, warrants more careful consideration than has been allotted to it in the past. For this reason, the case history records of 139 infants under 1 year of age who have died from accidental mechanical suffocation from January, 1939, to December, 1943, have been reviewed and are presented for discussion.*† Of these fatalities 119 (85 per cent) occurred in white infants; 19 (15 per cent), in Negro infants; and a single case, in a Chinese baby. In 80 per cent of these babies both parents were native-born. In most instances the families were of the lower income groups.

FACTORS CONTRIBUTING TOWARD ACCIDENTAL MECHANICAL SUFFOCATION

Age and Sex.—In Table III is shown the distribution of deaths according to age and sex. Eighty-five per cent of the fatalities occurred in infants under 6 months of age and 15 per cent, in those from 6 months to 1 year. Furthermore, the preponderance of deaths was in babies from 2 to 5 months (72 per cent) with the median age at death

This study was carried out under the direction of the Special Committee of Infant Mortality, Dr. Bret Ratner, Chairman, Medical Society of the County of New York.

*I wish to acknowledge with thanks permission granted by Dr. T. A. Gonzales, Chief Medical Examiner of the City of New York, to study the case history records of the babies in this series. Acknowledgment is also made of the assistance given by Mr. Leo Schneider in searching and completing the records.

†The term accidental mechanical suffocation as used here refers to occlusion of the external openings (nose and mouth) to the air passages by some object so that smothering occurs by obstructive cutting off of air supply. Deaths from accidental mechanical suffocation by choking from solid objects or liquids lodging in the air passages are not included. (Gonzales, T. A., Vance, M., and Halpern, M.: Legal Medicine and Toxicology, New York, 1937, D. Appleton-Century Co., Inc., p. 274.)

TABLE I*

DEATHS FROM ACCIDENTAL MECHANICAL SUFFOCATION ACCORDING TO AGE AND SEX IN THE REGISTRATION STATES OF THE UNITED STATES (INCLUDING DISTRICT OF COLUMBIA), 1933 TO 1942

YEAR	SEX	ALL AGES	UNDER 1 YR.	1 TO 4 YR.	5 YR. AND OVER
1933	Total	934	692	27	215
	M	553	344	12	197
	F	381	348	15	18
1934	Total	1124	834	21	269
	M	704	451	13	240
	F	420	383	8	29
1935	Total	1230	875	27	328
	M	791	475	17	299
	F	439	400	10	29
1936	Total	1408	1007	36	365
	M	908	560	20	328
	F	500	447	16	37
1937	Total	1341	970	35	336
	M	885	574	13	298
	F	456	396	22	38
1938	Total	1269	1004	34	231
	M	780	565	18	197
	F	489	439	16	34
1939	Total	1226	1008	37	181
	M	744	570	23	151
	F	482	438	14	30
1940	Total	1489	1224	35	210
	M	876	685	16	175
	F	613	559	19	35
1941	Total	1523	1263	60	200
	M	933	721	42	170
	F	590	542	18	30
1942	Total	1581	1333	49	199
	M	977	777	29	171
	F	604	556	20	28

*Compiled from Mortality Statistics and from Vital Statistics of the United States, U. S. Dept. of Commerce, U. S. Government Printing Office, Washington, D. C.

from 2 to 3 months. There was also a marked difference in deaths according to sex. Of the 139 fatalities, 69 per cent were in male babies and 31 per cent, in female babies. Thus, even in deaths from accidental mechanical suffocation the universal phenomenon of excess mortality in the male sex holds true.

Season of Accident.—The monthly variations in these deaths are shown in Fig. 1. It is not surprising that the peak of fatalities from accidental smothering took place during the winter months when more crib and carriage coverings are used to protect babies against the cold. This aspect of the problem will be discussed later.

Hour of Accident.—As will be readily understood, the exact hour of accidental suffocation could not be set with accuracy. In Fig. 2 is indicated the approximate time intervals at which the bodies were found after smothering took place. A sharp rise in deaths is evident between the hours from 3 A.M. to 6 A.M. and 6 A.M. to 9 A.M. This increase is worthy of note when considered in connection with the 2 A.M.

TABLE II*

DEATHS FROM ACCIDENTAL MECHANICAL SUFFOCATION ACCORDING TO AGE AND SEX, NEW YORK CITY, 1934 TO 1943

YEAR	SEX	ALL AGES	UNDER 1 YR.	1 TO 4 YR.	5 YR. AND OVER
1934	Total	33	20	1	12
	M	19	11	0	8
	F	14	9	1	4
1935	Total	36	26	2	8
	M	22	14	2	6
	F	14	12	0	2
1936	Total	49	36	2	11
	M	31	20	1	10
	F	18	16	1	1
1937	Total	28	25	0	3
	M	21	18	0	3
	F	7	7	0	0
1938	Total	33	28	2	3
	M	17	14	0	3
	F	16	14	2	0
1939	Total	34	25	3	6
	M	24	19	1	4
	F	10	6	2	2
1940	Total	45	38	3	4
	M	26	21	1	4
	F	19	17	2	0
1941	Total	43	35	3	5
	M	25	20	3	2
	F	18	15	0	3
1942	Total	56	51	3	2
	M	37	33	3	1
	F	19	18	0	1
1943	Total	45	43	2	0
	M	33	32	1	0
	F	12	11	1	0

*Compiled from Vital Statistics Tables, Bureau of Vital Records and Statistics, New York City Department of Health, Mr. Thomas J. Duffield, Registrar of Records.

and 6 A.M. feeding hours of the young infants and the times when adult members of the household are usually asleep.

Vehicle of Suffocation.—A study of the vehicles in which smothering occurred reveals that death took place mainly in cribs (35 per cent) and in the mothers' beds (15 per cent) during the morning hours (Table IV). In the afternoon and night hours the accidents ensued after placing the babies in carriages (23 per cent) and in cribs (19 per cent).

Suffocating Agents.—In Table V is listed the various agents found covering the heads of the babies or in occluding contact with the noses and mouths. In the crib, loose pillows, improperly applied blankets and mattress coverings (linen sheets and rubber sheetings), and mattresses were the common lethal agents. In the carriage, the unnecessary decorative pillows and coverings acted as the main agents in smothering. As has been previously noted, during the morning hours 15 per cent of the infants met death from overlaying after having been taken

for feeding into the mothers' beds. The smothering agent was either the mother's breast or upper extremity.

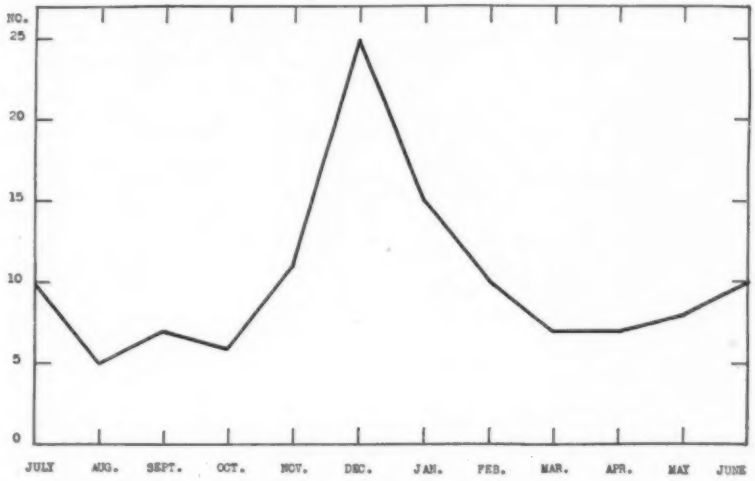

Fig. 1.—Accidental mechanical suffocation in infants under 1 year of age according to month of fatality.

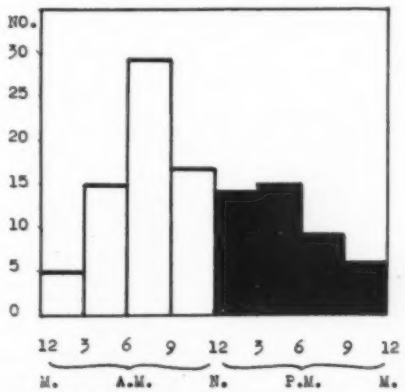

Fig. 2.—Time (hour) at which bodies of infants were found after occurrence of suffocation.

Posture in Relation to Suffocation.—

A. The "Face-Down" Posture: In Table VI are given the several postures in which the babies were found after accidental death. The "face-down" or prone posture was noted in 68 per cent of the fatalities. Of these babies 46 per cent were discovered with the noses and mouths in occluding contact with the lethal agents, usually soft pillows, mattresses, or mattress coverings. No additional agents covered the heads. In the remaining 22 per cent of the babies found "face-down," not only

TABLE III

DEATHS FROM ACCIDENTAL MECHANICAL SUFFOCATION IN 139 INFANTS UNDER 1 YEAR (ACCORDING TO AGE AND SEX)

AGE (MO.)	SEX	NUMBER	PER CENT
0 to 1	Total	14	10.0
	M	8	6.0
	F	6	4.0
1 to 2	Total	24	17.0
	M	14	10.0
	F	10	7.0
2 to 3	Total	34	25.0
	M	26	19.0
	F	8	6.0
3 to 4	Total	24	17.0
	M	17	12.0
	F	7	5.0
4 to 5	Total	18	13.0
	M	16	12.0
	F	2	1.0
5 to 6	Total	4	3.0
	M	1	1.0
	F	3	2.0
6 to 12	Total	21	15.0
	M	13	9.0
	F	8	6.0
	Total	139	100.0
	M	95	69.0
	F	44	31.0

TABLE IV

VEHICLE OF SUFFOCATION IN 125 CASES OF ACCIDENTAL MECHANICAL SMOTHERING IN INFANTS UNDER 1 YEAR (ACCORDING TO TIME OF ACCIDENT)

VEHICLE	TIME (HR.)			
	A.M.		P.M.	
	NUMBER	PER CENT	NUMBER	PER CENT
Crib	44	35.0	23	19.0
Carriage	9	7.0	29	23.0
Mother's bed	19	15.0	1	1.0
Total	72	57.0	53	43.0

TABLE V

AGENTS CAUSING SMOTHERING

AGENTS	VEHICLES		
	CRIB	CARRIAGE	MOTHER'S BED
Blankets or coverings	34	13	0
Pillows	17	14	1
Mattresses	20	6	0
Mattress coverings (sheets, pads, rubber sheetings)	12	6	0
Mother (overlaying)	0	0	19
Sleeping bag	1	0	0
Crib (wedging between sides)	1	0	0
Carriage (wedging between sides and hood)	0	1	0
Bib	1	0	0

TABLE VI

POSTURES IN WHICH 128 BABIES WERE FOUND AFTER SUFFOCATION (ACCORDING TO VEHICLE OF DEATH)

	VEHICLE	NUMBER	PER CENT
I. Postural Suffocation			
A. Face down or prone:			
1. Nose and mouth in contact with suffocating agent	Crib	44	35.0
	Carriage	13	10.0
	Mother's bed	1	1.0
2. Nose and mouth in contact with one suffocating agent and head covered by another agent	Crib	17	13.0
	Carriage	12	9.0
B. Face up or recumbent:			
Face covered by lethal agent	Crib	14	11.0
	Carriage	8	6.0
II. Overlaying	Mother's bed	19	15.0

were the noses and mouths in occluding contact with the instruments of death but the heads were also covered by accessory agents, such as pillows or blankets. In passing, it should be pointed out that the predominant number of infants found in the prone posture fell into the age group below 5 months (Table VII).

TABLE VII

POSTURE AT SUFFOCATION IN RELATION TO AGE AT DEATH

AGE	FACE DOWN		FACE UP		MOTHER'S BED (OVERLAYING)	
(MO.)	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
0 to 1	5	4.0	3	2.0	5	4.0
1 to 2	11	9.0	5	4.0	7	6.0
2 to 3	26	20.0	3	2.0	4	3.0
3 to 4	16	13.0	5	4.0	3	2.0
4 to 5	12	9.0	1	1.0	0	0.0
5 to 6	4	3.0	0	0.0	0	0.0
6 to 12	13	10.0	5	4.0	0	0.0
Total	87	68.0	22	17.0	19	15.0

B. The "Face-Up" Posture: In 17 per cent of the fatalities, the "face-up" or supine posture was noted with the smothering agents completely covering the babies' faces. These agents were most commonly pillows and loosened blankets.

C. Overlaying: The next most frequent cause of smothering was by overlaying. This form of accidental death occurred in 15 per cent of the infants and mainly involved those from 2 weeks to 3 months of age. Smothering usually followed the removal of the infant from its crib to the mother's bed for the 2 A.M. or 6 A.M. feedings. Accidental death was brought about by occlusion of the infant's nose and mouth either by the breast or by one of the upper extremities of the mother who had fallen asleep. Occasionally, the infant was wedged in between both sleeping parents.

COMMENT

To summarize, then, this study of accidental mechanical suffocation in infants under 1 year of age has disclosed the following circumstances underlying death:

1. The preponderance of deaths by smothering (85 per cent) occurred in infants under 6 months with the median age at death between 2 and 3 months.

2. Male babies showed a greater frequency of deaths (69 per cent) than female babies (31 per cent).

3. The peak of fatalities was reached during the late fall and early winter months, November through January.

4. When considered in relation to feeding hours, death from smothering took place most often between the hours from 3 A.M. to 6 A.M., and 6 A.M. to 9 A.M.

5. During the morning hours 35 per cent of the accidents occurred in cribs and 15 per cent in the mothers' beds. In the afternoon and night hours baby carriages and cribs were almost equally divided as the sites of accident.

6. In order of frequency the following were the smothering agents: (1) In the crib: blankets or outer coverings, mattresses, pillows, mattress coverings (sheets, pads and rubber sheetings); (2) in the carriage: pillows, blankets or outer coverings, mattresses and mattress coverings; (3) in the parent's bed: the mother's breast or upper extremity.

7. The posture most frequently noted on discovery of the infants' bodies was the "face-down" or prone posture (68 per cent). Fifty-five per cent of these infants were under 5 months of age.

8. In only 17 per cent of the fatalities were the bodies found in the "face-up" posture. Almost all these infants were 5 months of age and under.

9. In 46 per cent of the babies found in the "face-down" posture a single agent (pillow, mattress, or mattress covering) was in occluding contact with the noses and mouths, while in 22 per cent an added agent (pillow or blanket) covered the heads.

10. In the "face-up" posture pillows and blankets were found covering the infants' faces.

11. Death from overlaying comprised 15 per cent of the fatalities from smothering and involved very young infants from 2 weeks to 3 months of age. These accidental deaths occurred most frequently during the early morning hours.

MEASURES OF PREVENTION

Public Health Education.—Naturally, the circumstances comprising the settings for accidental mechanical smothering in infancy immediately call to mind obvious remedial measures. The increasing occurrence of this form of accidental death in infancy should be more widely

publicized both in medical and in lay periodicals. Vigorous efforts should be made by public health agencies to acquaint parents, nurses, physicians, and others concerned with the care of infants with the hazards to which these babies are unwittingly exposed.

It is not generally appreciated that the chief cause of accidental death in early infancy is mechanical suffocation. This cause of death has reached a point where it exacts an annual toll of lives of infants under 1 year of age exceeding that from burns and other accidental fatalities. Lack of apprehension of this situation may be due in part to the infrequency with which the practicing physician and the hospital are called upon to attend these accidental cases of smothering. The investigation of such deaths falls within the province of the local police department and the office of the medical examiner. Stress is placed on determining the existence of suspicious violence. The data from these inquests are treated as strictly confidential and the details responsible for death are rarely reported in the medical literature.

Care of the Infant.—The extreme youth of the victims of accidental smothering emphasizes the constant attention which must be afforded these babies at all hours during the day and night. No item of care can be overlooked if deaths from suffocation are to be avoided. In the nursing supervision of the baby heed should be paid to the following details:

1. Wearing Apparel: (1) Sufficient clothing should be provided to maintain normal body temperature, but excessive bundling should be avoided. (2) Free and unhampered movement should be allowed the baby at all times. (3) Constrictions about the neck such as are caused by the tapes of caps or bibs or by tight collars of dresses and outer garments should be eliminated. (4) Sleeping bag garments with mechanical closing and locking devices which may catch directly beneath the infant's neck should be prohibited.

2. The Crib and Carriage: Greater attention should be paid to the preparation of the infant's crib and carriage. (1) No infant should ever sleep on a pillow, but always on a flat mattress. (2) Rubber sheets and undersheets should be spread smoothly and be sufficiently large to allow tight tucking beneath the mattress. (3) Quilted pads should be bound down or pinned down to prevent loosening. (4) Oversheets and blankets should be large enough to permit firm tucking beneath the sides and lower edge of the mattress, but at the same time not so tight as to prevent freedom of movement of the baby. (5) Unnecessary articles such as decorative pillows, odd unattached blankets, strings or bars from which toys are dangled, and restraining straps which may slip up about the neck should be eliminated.

3. Feeding: Considerable care should be exercised in the management of the infant during and after feeding hours when not only smothering but also choking can occur from aspiration of regurgitated food. (1) No practice should be more emphatically condemned than

that of placing for feeding the unattended infant in its mother's bed where death from overlaying may be caused by the mother who falls asleep. (2) Throughout feeding the infant should be held in the mother's or nurse's arm with the attendant properly seated. (3) In artificially fed infants the practice should likewise be condemned of feeding the baby unattended in its crib by propping up the bottle in the infant's mouth. (4) After feeding the infant should be held up for sufficient time to allow escape of the "air-bubble" and then be placed down gently on his back, not stomach, with the head temporarily elevated. (6) The frequent occurrence of smothering directly after feeding, particularly during the early morning hours, strongly indicates that the infant should not be left unguarded too soon after completion of a feeding.

4. Position of Baby in Crib and Carriage: One other factor of importance merits consideration with regard to the position the baby is put while in the crib or carriage. It is common nursing practice to place the infant in the "face-down" or prone position. This detail of nursing care has been carried out by mothers and nurses for the following reasons: Firstly, it is believed that the baby is more comfortable and falls asleep easily. Secondly, the procedure is recommended to prevent the flattening deformity of the skull or cranial asymmetry which results from continued rest in the recumbent posture.[3] This nursing procedure may be expedient during the hours when the infant is under constant watch. But consider the risks involved when the baby is left unguarded. Attention should again be called to the preponderance of infants under 5 months of age who were found in the "face-down" posture on death from smothering.

Explanation for the more frequent incidence of smothering among young infants who are placed in the prone position is probably found by studying their behavioral schedules with respect to motor development. According to Gesell[4] and others,[5] during the third week of life about 80 per cent of infants exhibit head turning movements from left to right when in the prone posture. Thereafter, this phase of cephalic motor activity shows a decrease in frequency and is superseded at about the ninth week by head and chin lifting off the table top or bed. At this time the duration of such movements is brief, lasting but a minute. It is not until the fourth to the sixth month that head and chin raising movements become established with, however, limited duration and strength of these activities. It should also be borne in mind that the appearance of body turning or rolling movements have not begun.

It is, therefore, not surprising that of the infants under 6 months of age who died from accidental smothering so many were found in the "face-down" position in which they were previously placed. Head- and chin-lifting motor activities are not sufficiently developed to overcome the suffocating weight of the pillow or the blanket over the baby's head; nor are they of sufficient duration and strength to prevent con-

tinued occluding contact of the nose and mouth with the surface of the mattress to the point of smothering. It seems reasonable, therefore, to recommend that the routine nursing practice of placing infants in the prone position be avoided except during such times as the babies are constantly attended. The practice should, furthermore, be entirely done away with at night.

SUMMARY

Attention is called to the excessive number of infants under 1 year of age who are dying from accidental mechanical suffocation. These fatalities have shown a progressive increase each year to the point where accidental mechanical smothering now holds the dubious distinction of being the leading cause of accidental death in early infancy. Yet astonishingly little concern has been evinced with regard to the problem by public health workers and the literature contains but few comments. Concerted efforts should be made to study the problem completely and a constructive program should be designed and disseminated to prevent deaths from accidental mechanical suffocation.

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THE USE OF PROSTIGMINE AND A MODIFIED KENNY TECHNIQUE IN THE TREATMENT OF POLIOMYELITIS

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INTRODUCTION

ACUTE anterior poliomyelitis is a systemic, infectious disease which has been known and recognized for but a comparatively short period of time. A textbook published in 1784 by Underwood (London), gives a somewhat vague description of the disease under the name of *Debility of the Lower Extremities.* Within the past century Heine[1] first considered the condition a clinical entity, and Medin[2] first studied an epidemic of the disease (Heine-Medin's disease). However, it was not until 1894 that Caverly[3] in Vermont described the disease in this country. Since that time poliomyelitis has been given an ever-increasing amount of careful attention, especially in respect to its etiology, pathology, and epidemiology.

Nevertheless, it is astonishing that comparatively little clinical research which has proved valuable can be applied to the actual treatment of this debilitating and crippling disease. This undoubtedly is due to the fact that it is almost universally recognized now that the condition is due to a filtrable virus, and the treatment of virus diseases is generally unsatisfactory at best. Despite this, no one can deny that vast amounts of time and energy, to say nothing of the cost, have been expended in experimenting with various physical means designed to limit as much as possible the paralytic end results.

KENNY METHOD

More than thirty years ago a nurse in Australia came into her first contact with poliomyelitis. This nurse, the now well-known Sister Elizabeth Kenny, sought advice from a physician as to how to treat this condition and was told that treatment of the acute stage was in general most discouraging. According to her own statement[4] she observed that patients afflicted with the disease exhibited an involuntary shortening of some of the muscles of the body. Any attempt to correct this condition resulted in an exaggeration of the shortening and intense pain. In order to become rid of the "spastic" condition of the muscles, Kenny applied moist heat. Following this, the concepts, now generally known (even though not universally accepted), of mental alienation and incoordination were introduced. It is not the purpose of this paper to enlarge upon the Kenny method per se, but the pertinent points and our modifications thereof will be discussed later.

MATERIAL AND METHODS

Since the fall of 1941 a large percentage of cases of poliomyelitis, either suspected or actual, occurring in the state of Delaware have been admitted to the Doris Memorial Unit of the Wilmington General Hospital. All such patients have been subjected to the Kenny method of treatment or some modification thereof. More recently we have adopted the use of prostigmine,* a synthetic parasympathicomimetic preparation. We have had all necessary facilities for investigation placed at our disposal, including the services of several Kenny-trained technicians.

To date some forty-three patients with poliomyelitis have been observed, the great majority of which have been children 10 years of age or younger. There were only three adults, two cases occurring in 1941 and one in 1942. Twenty-one cases form the basis of this report, all of the patients receiving treatment with the Kenny technique, a modification thereof and/or prostigmine. (Table I.) Both acute and chronic cases are included in this group. Muscle and joint motion measurements were made in all instances at periodic intervals.

Our modification of the Kenny technique consisted of the elimination of the hot packs and the substitution of prostigmine, usually orally but occasionally parenterally as well. No change was made in the usual muscle re-education methods, nor in the passive joint movement procedure.

These cases have been tabulated in Table I, and a few of the more interesting and instructive case histories presented below. Unless otherwise noted, all patients received the modified Kenny method of treatment, general supportive medication to prevent anemia and anorexia (iron and thiamine), mild sedation (phenobarbital) when necessary, in addition to prostigmine which was given as described.

CASE REPORTS

CASE 1 (279).—P. P., a female, aged 6 years; was admitted Aug. 30, 1943, and discharged Nov. 28, 1943.

The parents stated that the child was well until five days before admission at which time she complained of a stiff neck. The following day a pain in the right shoulder developed and she was found to have a temperature of 101° F. by rectum. The day before admission the shoulder pain disappeared, and the temperature dropped to 100° F., but she was unable to walk or stand on the right leg although there was no pain.

The past and family histories were irrelevant.

On admission the patient appeared to be a well-developed and nourished female child, not acutely ill and in no obvious pain. The rectal temperature was 101° F.; pulse rate, 116 per minute and respirations, 24 per minute. The eyes, ears, nose, and throat were not remarkable. There was some nuchal rigidity and any attempt to flex the neck anteriorly resulted in considerable pain. The heart, lungs, and abdomen presented no abnormalities.

*Prostigmine methylsulfate and prostigmine bromide, used in this investigation, were kindly supplied by Hoffmann-La Roche, Inc., Nutley 10, N. J.

TABLE I

CASE	INITIALS	SEX	AGE	DATE OF ONSET	TYPE OF DISEASE	INVOLVEMENT	PREVIOUS THERAPY AND DURATION	DATE PROSTIGMINE STARTED	NUMBER DAYS ON PROSTIGMINE THERAPY	TOTAL AMOUNT PROSTIGMINE BROMIDE (MG.)	TOTAL AMOUNT PROSTIGMINE METHYL SULFATE (MG.)	END RESULT AND COMMENT
1	P. P.	F	6	8/25/43	Acute	R.L.E.	None	8/30/43	50	4035	11.5	Excellent; can walk without limp
2	R. T.	M	15	9/16/43	Acute	R.L.E. L.L.E. R.U.E.	None	9/21/43	41	4470	23	Good; prostigmine again started 1/22/44 to further relax right arm
3	G. N.	M	9	8/26/43	Acute	R.U.E.	None	8/30/43	75	6570	13	Excellent
4	W. B.	M	9	9/ 6/43	Acute	R.L.E. L.L.E.	None	9/ 6/43	43	3720	–	Excellent; no residual effects
5	L. M.	M	5	8/18/43	Subacute	L.L.E.	None	9/21/43	51	3750	–	Good
6	G. R.	F	7	7/ 4/42	Chronic	R.L.E. L.L.E.	Kenny, 11 mo.	6/28/43	86	3180	44.5	Marked improvement with prostigmine; walks with sticks
7	R. B.	M	2	9/15/41	Chronic	L.L.E.	Orthodox (cast), 4 mo.; Kenny, 11 mo.	9/24/43	20	600	–	Greatly increased strength of left leg following prostigmine
8	A. B.	M	10	9/22/40	Chronic	R.L.E. L.L.E.	Orthodox (brace) 30 mo.; Kenny, 4 mo.	7/ 8/43	61	2700	23.5	Excellent, patient walks very well with aid from sticks
9	G. J.	M	31	9/26/42	Chronic	L.U.E. R.L.E. L.L.E. Diaphragm	Kenny, 11 mo.	7/ 1/43	68	3420	4.5	Excellent, walked well without aid of sticks for first time following prostigmine
10	D. C.	M	4	10/19/41	Chronic	L.L.E.	Orthodox (splints and braces), 12 mo.; Kenny, 8 mo.	6/28/43	112	7290	32.5	Good; walked without aid on day after prostigmine was first given; patient did not cooperate when discharged and lost much of his improvement

L.U.E. left upper extremity
R.U.E. right upper extremity
L.L.E. left lower extremity
R.L.E. right lower extremity
Kenny hot packs.

11	J. B.	M	14	9/26/42	Chronic	R.L.E. Diaphragm	Kenny, 9 mo.	6/28/43	34	3000	-	Good; definitely increased relaxation
12	M. S.	M	3	8/17/42	Chronic	L.U.E.	Kenny, 4 mo.	7/ 1/43	15	1350	-	Excellent; spasm relieved with prostigmine
13	J. R.	M	7	10/ 1/42	Chronic	L.U.E.	Kenny, 8 mo.	7/ 1/43	30	2700	-	Excellent; spasm in shoulder completely gone
14	J. D.	M	9	10/19/42	Chronic	R.L.E. Trapezius	Kenny, 5 mo.	7/ 1/43	30	750	-	Excellent; spasm in neck muscles rapidly relieved
15	H. M.	M	5	9/12/42	Chronic	Nonparalytic trapezius spasm	Kenny, 2 mo.	7/ 2/43	17	1500	-	Excellent; spasm in neck muscles abolished
16	N. N.	F	14	9/26/42	Chronic	R.L.E. R.U.E. Diaphragm	Kenny, 8 mo.	9/11/43	10	450	-	Excellent; spasm in cervical muscles rapidly relaxes
17	F. R.	M	10	10/18/41	Chronic	L.L.E.	Kenny, 1 mo. Orthodox, 12 mo. Kenny, 7 mo.	6/28/43	10	600	5	Excellent, pronounced relaxation of muscles with prostigmine therapy
18	J. M.	F	15	7/ 7/41	Chronic	R.L.E. L.L.E.	Crutches; orthodox (cast) and (braces) 28 mo.	9/ 8/43	83	7650	26	Excellent; walks without braces; able to walk without any aid
19	D. R.	M	5	10/12/41	Chronic	R.L.E.	Kenny, 2 mo. Orthodox, 16 mo.	6/28/43	20	900	2.5	Excellent; relaxation and coordination of muscles much better after prostigmine
20	J. van P.	F	16	10/14/41	Chronic	R.L.E. L.U.E. L.L.E.	Kenny, 2 mo. Orthodox, 18 mo. (braces)	6/27/43	60	3600	55	Excellent; shoulder normal; walking without braces
21	J. McC.	F	15 mo.	9/15/43	Subacute	L.L.E.	None	11/23/43	20	600	-	Good; walking improved

Examination of the neuromuscular system revealed normal upper extremities. The left lower extremity was normal in all respects. The right leg and thigh exhibited a flaccid paralysis. The right foot could be fully flexed and extended, but there was loss of adduction, flexion, and extension at the hip. Some abductive power remained. The hamstring muscles were tight. The Achilles reflex was the only one present on the right. (Fig. 1.)

Fig. 1.—Case 1.

Laboratory Findings.—Laboratory findings disclosed: hemoglobin on admission, 13.0 Gm. per cent; erythrocyte count, 4.5 millions per cubic millimeter; leucocyte count, 8,200 with 76 per cent polymorphonuclear neutrophiles and 24 per cent small lymphocytes. Rachiocentesis revealed a clear fluid under slightly increased pressure, 65 leucocytes per cubic millimeter and a normal amount of sugar and globulin. Urinalysis was essentially normal.

Course in Hospital.—The course of treatment and results were as follows:

Aug. 30, 1943, Prostigmine methylsulfate, 0.5 mg., and atropine sulfate, $\frac{1}{200}$ grain were given subcutaneously twice.

Aug. 31, 1943, Tenderness in both gastrocnemii and marked fasciculation of hamstrings was noted. Lordosis and nuchal rigidity were somewhat increased. Some improvement in flexion of right leg was noted. Atropine sulfate was discontinued because of marked dilatation of pupils, but administration of 0.5 mg. prostigmine methylsulfate was increased to four times daily in addition to 15 mg. prostigmine bromide by mouth three times daily.

Sept. 1, 1943, There was slight relaxation in back muscles. The patient could flex right leg voluntarily. Prostigmine methylsulfate, 0.5 mg., was given three times daily, plus 15 mg. prostigmine bromide also three

times daily. (The prostigmine was continued until Sept. 6, 1943, at which time 15 mg. prostigmine by mouth was given twice daily until Oct. 18, 1943, when all medication was discontinued.)

Sept. 2, 1943, The patient was still unable to raise the head, but back muscles were more relaxed. The patient could flex the right thigh and extend the leg. There was marked fasciculation in hamstrings.

Sept. 3, 1943, The patient could raise the head two inches from the bed. The right knee angle was 120 degrees; the left knee, 112 degrees;

Fig. 2.—Case 1.

the right posterior ankle, 82 degrees; the left posterior ankle, 77 degrees; the right anterior ankle, 114 degrees; the left anterior ankle, 110 degrees.

Sept. 4, 1943, There was more muscle relaxation, although the patient complained of pain in the right ankle when the foot was inverted.

Sept. 8, 1943, The right knee was 108 degrees; the left, 117 degrees; the right posterior ankle, 101 degrees; the left posterior ankle, 97 degrees; the right anterior ankle, 109 degres; the left anterior ankle, 118 degrees. The patient could raise the head four inches from the bed (Fig. 2).

Sept. 15, 1943, The relaxation of the muscles was increasing steadily.

Oct. 15, 1943, Improvement was continuing steadily.

Nov. 28, 1943, the patient was discharged in good condition. Walking was accomplished without a limp, but with the aid of orthopedic shoes and arch supports. All movements of the right lower extremity were normal, but there appeared to be a definite weakness in adduction and abduction of the right thigh. The abdominal muscles were weak in that the patient could not arise erect from the supine position.

Follow-up Record.—Subsequent examinations revealed the following:

Jan. 31, 1944, The abdominal musculature was considerably improved, the patient being able to arise to the sitting position without aid. The

anterior tibial muscles were in good condition except for a slightly thinner tendon on the right. (Fig. 3.)

March 1, 1944, The patient was in very good physical condition. The abdominal muscles were much stronger. There was a 4 cm. circumferential loss due to atrophy of the right thigh as compared with the left, and between 1 and 2 cm. loss in the right leg.

Fig. 3.—Case 1.

CASE 3 (275).—G. L. N., male, aged 9 years, was admitted Aug. 31, 1943, and discharged Nov. 29, 1943.

Five days before admission the patient complained of pain and inability to use the right arm. The next day "feverishness" was noted, followed by a generalized headache and pain in the right shoulder. Two days before admission it was observed that the patient was unable to raise the right arm above the shoulder level, and complete flexion of the right arm was impossible.

The past and family histories were irrelevant.

On admission the temperature was 101° F. by rectum; pulse rate, 128 per minute; and respirations, 24 per minute. There was observed evidence of fair nutrition and development. The face was flushed and eyes appeared "febrile." Ears, nose, and throat were not remarkable, and there was marked stiffness of the neck. Heart, lungs, and abdomen presented no notable findings.

Neuromuscular examination revealed considerable fasciculation of the entire right side. There was moderate "cupping" of the shoulders, especially on the right. The left upper extremity showed slight weakness with inability to abduct and raise the arm at the shoulder. The right arm was unable to be maintained aloft, and the right biceps and triceps were weakened. Abduction and adduction were incoordinated. The

knees were slightly raised; the right knee angle was 104 degrees; the left knee angle, 108 degrees. The right anterior ankle was 107 degrees. The reflexes were essentially normal. (Fig. 4.)

Laboratory Findings.—Laboratory findings disclosed hemoglobin, 12 Gm. per cent with a red blood cell count of 4.5 millions per cubic millimeter; leucocyte count, 5,500 per cubic millimeter with 84 per cent polymorphonuclear neutrophiles and 16 per cent small lymphocytes. Rachiocentesis revealed a clear fluid with 28 white cells per cubic millimeter, normal globulin; and no growth on culture. The urine was normal.

Fig. 4.—Case 3.

A diagnosis of acute anterior poliomyelitis was made and "routine" therapy initiated. In addition, the patient received 0.5 mg. prostigmine methylsulfate two or three times daily for ten days, followed by 30 mg. prostigmine bromide by mouth three times daily for seventy-four days (until Nov. 13, 1943). No untoward effects were observed except for occasional nervousness which could be alleviated with phenobarbital or atropine.

Course in Hospital.—The course of treatment and results were as follows:

Aug. 31, 1943, There were marked fasciculations in right pectoral and hamstring areas and less rigidity of the neck; the patient could raise the head three and one-half inches from the bed. The left biceps were somewhat improved.

Sept. 1, 1943, The patient could move the left arm more.

Sept. 4, 1943, The temperature, pulse rate, and respiration were normal. The patient could raise the head four inches from the bed. The right knee angle was 107 degrees; the left knee, 108 degrees; the right anterior ankle, 107 degrees and the right posterior ankle, 83 degrees.

Sept. 5, 1943, The temperature was 100.4° F. by rectum. There was definite relaxation of spasm in the right arm and both legs. The patient was improving steadily with prostigmine. (Fig. 5.)

Sept. 11, 1943, The relaxation of spasm in involved muscles was increasing daily. Progress was exceptionally favorable. The right knee angle was 99 degrees; the left knee, 116 degrees; right anterior ankle, 110 degrees; the left anterior ankle, 105 degrees.

Sept. 21, 1943, Neck rigidity had almost disappeared. The patient seemed to be improving slowly but steadily.

Oct. 2, 1943, Some spasm still persisted in the legs. There was almost complete return of function of the right arm. The patient's improvement with prostigmine was definite.

Nov. 29, 1943, The patient was discharged to return to the outpatient clinic. The left shoulder was fully recovered. The right upper extremity was still somewhat weakened. The lower extremities were normal.

Follow-up Record.—A subsequent examination, Feb. 1, 1944, revealed a moderate degree of atrophy of the right deltoid, supra- and infraspinatus. The function of the deltoid (right) was poor; coracobrachialis, fair.

Fig. 5.—Case 3.

CASE 2 (286).—R. T., male, aged 15 years, was admitted Sept. 20, 1943, and discharged Nov. 30, 1943.

The past and family histories were irrelevant.

Four days before admission the patient awoke with a backache which persisted throughout the day. The following day he noticed that his legs were beginning to weaken and that he had no control over them. The day prior to admission, upon attempting to get out of bed, he collapsed, his legs being quite powerless. Meanwhile the bachache continued and, in addition, headache and nuchal rigidity developed.

On admission to the hospital the patient appeared to be well-developed and nourished. The temperature was 99° F. by mouth; pulse rate, 88 per minute; and respirations, 20 per minute. The eyes, ears, nose, and throat were not remarkable. Swallowing was carried out normally.

The neck was rigid and the head could be raised only two inches from the bed.

The heart, lungs, and abdomen showed no abnormalities. The chest expansion was limited.

The entire back was rigid and any attempt at passive flexion elicited intense pain. The right upper extremity was apparently paralyzed.

The lower extremities were seemingly paralyzed save for some slight motion of the toes. There was considerable spasm of the gastrocnemii and hamstrings.

Laboratory Findings.—Laboratory findings disclosed hemoglobin, 14 Gm. per cent; erythrocyte count, 5 millions per cubic millimeter; leucocyte count, 11,900 with 83 per cent polymorphonuclear neutrophiles and 17 per cent small lymphocytes.

Urinalysis revealed no abnormalities.

Rachiocentesis revealed a crystal clear fluid under slightly increased pressure. There were 4 leucocytes per cubic millimeter and no increase in globulin. Culture was sterile.

A diagnosis of acute anterior poliomyelitis was made and therapy started. In addition to the routine, the patient was given 1 mg. prostigmine methylsulfate subcutaneously three times daily for eight days. From Sept. 28, to Oct. 5, 1943, a period of one week, he received 45 mg. prostigmine bromide by mouth four times daily, and for the next month thereafter 30 mg. prostigmine bromide four times daily. Atropine sulfate, $\frac{1}{150}$ grain, was given with each subcutaneous dose of prostigmine methylsulfate and with each oral dose of prostigmine bromide.

This patient also received hot packs from Sept. 22 to Oct. 7, and again from Nov. 8, to Nov. 30, 1943. On Jan. 22, 1944, prostigmine bromide by mouth (30 mg. three times daily) was again started.

Course in Hospital.—The course of treatment and results were as follows:

Sept. 23, 1943, The general condition was much improved. The patient was able to flex the right forearm. The neck rigidity was less; the head could be raised four inches from the bed.

Sept. 30, 1943, The patient was more comfortable generally. The head could be raised five inches from bed. All extensors of the right upper extremity were weak.

Oct. 3, 1943, After consultation the neurologist reported:

> The patient talked a great deal, but found it difficult to answer a direct question briefly. The thought processes were slow, and there was restlessness with a suggestion of mild confusion. Most of these mental symptoms should clear up in time as he gains strength and improves.
>
> There was moderate atrophy of all muscles. Throat, speech, and respiratory functions and all extremities were affected with about 20 per cent grip in the left hand. The muscles were all sore to touch or movement. The sphincter muscles were also affected. There was incontinence of both bowels and bladder.
>
> The tendon reflexes were all absent except a slight reaction in the left upper extremity which was recovering best.
>
> Sleeplessnes would probably be helped best by trying to find the correct dose of phenobarbital, grains $\frac{1}{2}$ to $1\frac{1}{2}$.

About 5 minims tincture nux vomica in 2 ounces of water might help the appetite and give some tone to the muscles. A rest on the prostigmine for a week or two, and then a return to it again might prove helpful.

Oct. 7, 1943, The general condition had improved. The extension of the right hand was stronger. The patient was able to flex the right forearm and motion in all toes had improved.

Nov. 8, 1943, The patient had been nervous and restless and was incontinent of urine and feces. He did not like to cooperate with the nurses. The right forearm was fixed at a 90 degree angle. The right shoulder was elevated and fixed. There was marked atrophy of the entire body and no muscle power in the lower extremities save for the toes.

Nov. 13, 1943, The condition was unchanged. The appetite was poor.

Nov. 21, 1943, The patient had been complaining of numbness and pain in both legs. His mental attitude appeared to be very poor. He was restless and uncooperative.

Nov. 27, 1943, Hot packs for the past few days had relieved spasm of the flexor muscles of the right arm. The right wrist could be flexed and extended. The general condition had improved.

Nov. 30, 1943, The patient was improved and was discharged from the hospital.

Follow-up Record.—A subsequent examination, Jan. 22, 1944, revealed good function of muscles of the right upper extremity with exception of the right deltoid and coracobrachialis. Abdominal muscles and those of the right lower extremities were poor.

There was a slight scoliosis from the second to the eighth thoracic vertebrae. The vertebral border of the right scapula was 1.5 cm. closer to the spine than on the left.

Spasm of the right quadratus lumborum was causing an elevation of the pelvis on that side and an apparent shortening of the right lower extremity amounting to 0.5 cm.

The upper fibers of the right gluteus maximus were atrophied.

Straight leg raising (passive), 6 inches on the right and 7 inches on the left (midthigh region), was possible.

Right upper and both lower extremities were markedly atrophied.

Therapy recommended was the continuance of hot packs and prostigmine bromide, 30 mg., three times daily.

CASE 7 (317).—R. R. B., male, aged 2 years, was admitted Oct. 20, and discharged Dec. 20, 1942.

Present Illness.—Approximately one year before admission the patient became ill, developed a slight fever, vomiting and complained of a headache. Initially the family physician believed the condition was due to "teething." However, the temperature did not return to normal and on the fifth day, after using the nursery training chair, the left lower extremity crumpled under him in attempting to stand. Hospitalization was advised, where a rachiocentesis confirmed the suspicion of acute anterior poliomyelitis.

Three weeks after the onset the child was placed in a half-shell cast in which both lower extremities were maintained in the abducted position. (Fig. 6.) In this cast the child could not sit up or even hold his head erect. Baking and massage of the left leg and thigh was initiated on a three times weekly schedule.

Some four months after the onset, Jan. 19, 1942, the patient came under our care but was not hospitalized immediately. However, the cast was removed at once. Due to the prolonged immobilization the child was unable to flex the legs or thighs. The right leg and thigh muscles exhibited good tone. Those on the left were soft and flabby. Considerable spasm was noted in the hamstrings, quadriceps, and adductors. Foot drop was in evidence on the left. The gluteal musculature was in good condition bilaterally, the gluteal sulcus being prominent on both sides.

The upper extremities were essentially normal save for weakness and moderate atrophy on the left. The mother was instructed to apply hot packs to the left shoulder, lower back, both lower extremities and left foot. The packs were changed every fifteen minutes during the first week and every thirty minutes during the second week for twelve hours daily. Thereafter the packs were applied only to the lower back and left lower extremity.

Fig. 6.—Case 7.

Progress.—The progress recorded under this treatment was as follows:

Feb. 12, 1942, The general condition was improving slowly but steadily.

March 12, 1942, The patient could raise the left leg off the bed and could abduct and adduct it. Sitting erect and crawling were easily accomplished.

April 16, 1942, The child was now crawling on both knees with much more motion in the joints of the left lower extremity.

June 18, 1942, He could take good firm steps with someone holding his hands, the entire left lower extremity being raised from floor. Hot packs on the left lower extremity were applied at intervals. (Fig. 7.)

Oct. 20, 1942, The child was admitted to the Doris Memorial Unit of the Wilmington General Hospital for further observation and treatment.

Course in Hospital.—On admission to the hospital physical examination revealed no abnormalities save changes in the left lower extremity. The left iliopsoas was weak and somewhat tender, as were the abductors and hamstrings. Hyperextension of the left knee was noted when walking. There was complete "alienation" of the muscles in this part.

Oct. 30, 1942, Passive exercises were given with good results.

Nov. 20, 1942, Active exercise was encouraged.

Dec. 20, 1942, He was discharged from the hospital in greatly improved condition.

Progress.—The patient was followed at periodic intervals and although progress was very slow, it could be definitely seen that improvement was continuing. On Sept. 24, 1943 prostigmine therapy was initiated (Fig. 8), 7.5 mg., prostigmine bromide being given four times daily for three weeks. At the end of this period of time the patient exhibited remarkable improvement. There was greater strength than ever before in the left hamstrings and in the ability to raise the left foot and leg from the prone position. However, hyperextension of the left knee was more pronounced and on this account prostigmine therapy was discontinued temporarily.

Fig. 7.—Case 7.

On Nov. 5, 1943, when last seen, the child could walk quite well without aid although some of the left leg muscles were paralyzed. Moderate hyperextension of the knee persisted, being attributed to the paralyzed quadriceps and not to any treatment received.

Case 6 (259).—G. R., female, aged 7 years, was admitted July 10, 1942, and discharged July 30, 1943.

Present Illness.—Six weeks prior to admission the patient developed a sore throat and fever. A peritonsillar abscess was diagnosed and incised. Moderate drainage ensued and recovery was uneventful within ten days.

Following this the patient appeared well until six days before admission at which time she complained of a severe headache. The following

day this had disappeared, but the day after (four days before admission) the right leg felt weak and she could walk only with difficulty. A tentative diagnosis of acute anterior poliomyelitis was made and hot fomentations applied to the affected part. Two days before admission a rachiocentesis revealed a clear fluid under slightly increased pressure and 54 leucocytes per cubic millimeter. The day of admission a seeming paralysis developed in both legs.

The past and family histories were irrelevant.

Physical Examination.—Physical examination showed a well-developed, moderately nourished young white female child, lying quietly in bed, cooperative but apprehensive. The temperature was 99.3° F. by rectum; the pulse rate, 124 per minute; respirations, 22 per minute.

Fig. 8.—Case 7.

The head was normal except for marked internal strabismus of the right eye.

There was marked rigidity of neck with pain on attempt to flex.

The heart, lungs and abdomen were normal.

Neuromuscular examination revealed no abnormalities in the upper extremities.

The lower extremities showed considerable involvement. The only active motion was very slight flexion of the right toes and left knee. Passive motion of the legs was accomplished only with pain in the popliteal region and thigh. All deep reflexes were bilaterally abolished. Abdominal reflexes were absent on the right and greatly diminished on the left. Hypoesthesia was present over the entire right lower extremity.

Laboratory Findings.—Laboratory findings disclosed hemoglobin, 13.0 Gm. per cent with 5.1 millions erythrocytes per cubic millimeter; leu-

cocyte count, 8,500 with 66 per cent polymorphonuclear neutrophiles, 32 per cent small lymphocytes and 2 per cent monocytes. Urinalysis was essentially normal. Rachiocentesis was not repeated.

Course in Hospital.—The course of treatments and results were as follows:

July 11, 1942, The patient was able to void only after warm saline enema. All abdominal reflexes were abolished. The toes on both feet could be moved slightly and the left leg was flexed to a slight degree.

July 13, 1942, Fomentations were applied to the abdomen and the affected parts. There was increased motion of the left leg.

July 16, 1942, Abdominal reflexes were present but sluggish. The lower extremity deep reflexes were still absent.

July 24, 1942, Active motion gradually returned in the left leg. There was less rigidity of the neck.

Hot fomentations to affected parts were continued.

Fig. 9.—Case 6.

July 30, 1942, The orthopedic surgeon in consultation advocated the continuation of the Kenny method.

Aug. 1, 1942, There was marked spasticity of the paravertebral muscles in the thoracolumbar area. The cervical vertebral muscles were less spastic than on admission. The patient, when requested to sit up, could arise to a 45 degree angle with the bed.

The upper extremities showed good active motion, but the right hand had a weaker grip than the left and there was diminished muscle strength in both the reflexors and extensors of the right upper extremity.

The lower extremities revealed an external rotation with bilateral foot drop. The flexion of the left leg was to 30 degrees. The left ankle jerk was the only deep reflex present. (Fig. 9.)

Measurements:

	RIGHT	LEFT
4 in. above tip of patella	10.25 in.	10.75 in.
4 in. below tip of patella	8.25 in.	8.25 in.

Aug. 20, 1942, Measurements:

	RIGHT	LEFT
4 in. above tip of patella	10.5 in.	10.75 in.
4 in. below tip of patella	8.25 in.	8.25 in.

Aug. 27, 1942, Measurements:

	RIGHT	LEFT
4 in. above tip of patella	10.5 in.	10.75 in.
4 in. below tip of patella	8.15 in.	8.15 in.

The patient could not move any portion of the right lower extremity. There was slight flexion of the right leg. There was no abduction or adduction of the thighs. Upper extremities revealed normal muscle strength.

Fig. 10.—Case 6.

Sept. 3, 1942, Temperature, pulse, and respirations were normal. The general condition was good. The Kenny therapy was being continued.

Sept. 6, 1942, Spasm persisted in the paravertebral muscles, the neck, and lower extremities.

Sept. 19, 1942, Muscle re-education was being continued. Spasm had lessened.

Oct. 2, 1942, No spasm was observed. There was slight limitation to the internal rotation of the right arm. Adductors of the thighs resisted passive motion to a slight degree, and there was a weakness of the glutei bilaterally. Flexion of the feet and legs was fairly good. Passive exercises were being continued.

Jan. 15, 1943, Flexion of both thighs was good and the patient could sit and stand erect without assistance.

April 1, 1943, Cervical and paravertebral muscles seemed normal. Weakness was noted in almost all the muscle groups of both lower extremities.

June 1, 1943, The patient could stand without aid with fairly good posture but walked with the aid of sticks. There was a generalized weakness of the lower extremity muscle groups. (Fig. 10.)

June 28, 1943, Prostigmine therapy was initiated because of lack of satisfactory progress. One-half milligram prostigmine methylsulfate with $\frac{1}{150}$ grain atropine was given three times daily (subcutaneously) for one month.

July 30, 1943, The patient was discharged from the hospital. Fomentations were discontinued for the first time since admission. The condition was markedly improved since initiation of prostigmine treatment.

Progress.—From Aug. 1 to Sept. 22, 1943, the patient received 15 mg. prostigmine bromide by mouth four times daily (a total of 3,180 mg.). She began to improve rapidly, especially in respect to relaxation of the gastrocnemii, soon after prostigmine was started. The left quadriceps as well as the remainder of the entire left lower extremity improved in muscle strength. Walking with the aid of sticks became much better. When last seen in November, 1943, she could walk without the aid of any appliance provided an assistant supported the right knee (paralysis of right quadriceps apparently complete).

CASE 20 (345).—J. van P., female, aged 16 years, was admitted Oct. 21, 1941 and discharged Dec. 22, 1941.

Present Illness.—Two weeks prior to admission the patient developed a headache, sore throat, and slight cough. This, coupled with a slight fever, was considered to be grippe but two days before admission the patient experienced some difficulty in sitting up. This increased until the day of admission when she was unable to lift her back from the prone position.

Past and family histories were irrelevant.

Physical Examination.—Physical examination revealed a well-developed and nourished adolescent white female, not acutely ill, lying quietly in the prone position.

The head revealed no abnormalities. The neck was slightly stiff. The heart, lungs, and abdomen were normal.

Neuromuscular examination revealed some weakness of the lower extremities, more pronounced on the left in the flexor group. Reflexes were normal except in the lower extremities where they were absent.

Laboratory Findings.—Laboratory findings disclosed hemoglobin, 15 grams per cent with 5.2 millions erythrocytes per cubic millimeter; leucocyte count, 7,300 per cubic millimeter with 81 per cent polymorphonuclear neutrophiles, 15 per cent small lymphocytes, 2 per cent monocytes, and 2 per cent eosinophiles. Urinalysis was normal.

A rachiocentesis revealed clear fluid under slightly increased pressure, 25 leucocytes per cubic millimeter (almost all lymphocytes), and a slight increase in the amount of globulin.

A diagnosis of acute anterior poliomyelitis was made and orthodox treatment with splints was instituted.

Course in Hospital.—The course of treatment with results follow:

Nov. 4, 1941, Muscle power of all affected groups was steadily increasing. Splints were removed from lower extremities, mainly because of pain on the pressure area of the left foot.

Nov. 20, 1941, Hot packs to legs, thighs, back and shoulders were applied.

Dec. 22, 1941, Muscle power in tibial group (bilaterally) was very weak, left hamstrings were quite weak, but the right was almost normal. The patient was discharged from the hospital to receive massage and passive exercise at home. All hot packs were permanently discontinued.

Progress.—The patient remained in bed at another institution from Jan. 12, until May 1, 1942. No hot packs were used and the only therapy was the customary muscle re-education and passive exercise.

Fig. 11.—Case 20.

June 30, 1942, Leg braces were fitted below both knees, walking with aid of braces was accomplished fairly well.

May 14, 1943, there was a slight trace of function in the left anterior tibial group, and left gastrocnemius with atrophy of the left leg and "alienation" of the right leg muscles. There was weakness of the hamstrings bilaterally and slight atrophy of both glutei maximi.

There was 0.5 inch elevation of the left scapula and a slight right thoracic scoliosis. The patient was unable to sit up from supine position.

June 26, 1943, She was admitted to our Kenny Clinic outpatient department for muscle re-education. (Fig. 11.)

June 27, 1943, Prostigmine therapy was initiated by giving 30 mg. prostigmine bromide by mouth three times daily and 1.0 mg. prostigmine methylsulfate with $\frac{1}{150}$ grain atropine sulfate daily by subcutaneous injection.

July 16, 1943, The elevation of the left scapula had regressed and the shoulder was normal as confirmed by comparative roentgenography. The scoliosis present before prostigmine therapy was started had completely disappeared.

The leg braces were removed and it was found that the patient could walk without aid except for the high top shoes which had formerly been attached to the braces.

July 27, 1943, The patient could walk barefooted without difficulty and without aid. Several muscles of the right leg had returned to power and the left leg showed signs of some muscular power. After four weeks of prostigmine therapy this patient showed far more improvement than had been made during the prior year of treatment with the modified Kenny technique. (Fig. 12.)

Fig. 12.—Case 20.

Sept. 4, 1943, All prostigmine therapy was discontinued.

Sept. 10, 1943, Correction of shoulder deformity and scoliosis was maintained without prostigmine. Walking could be carried out much more efficiently than before.

March 19, 1944, All improvement noted with prostigmine had been maintained. The patient was away for three months in California where she was married. All musculature and function was apparently normal except for poor toe and foot flexion on the left, and poor gastrocnemius action on the left. (Fig. 13.) She was able to sit up and bend over unassisted.

Case 19 (340).—D. R., male, aged 5 years; was admitted Oct. 18, and discharged Dec. 21, 1941.

Present Illness.—The present illness began five days prior to admission when the patient developed a slight fever with no other symptoms.

The following day it was noted that he was limping, and this condition gradually progressed up to the time of admission.

Past and family histories were irrelevant except for occasional attacks of bronchial asthma.

Physical Examination.—Physical examination revealed a well-developed and well nourished young white male child, lying quietly in bed, not acutely ill. Temperature on admission was 101.2° F. by rectum; pulse rate, 112 per minute; and respirations, 28 per minute.

Head, neck, thorax, and abdomen presented no abnormalities.

Neuromuscular examination revealed that the right leg could not be lifted to more than a 45 degree angle, the muscle power was markedly diminished and all tendon reflexes abolished. On the left there was no abnormality noted.

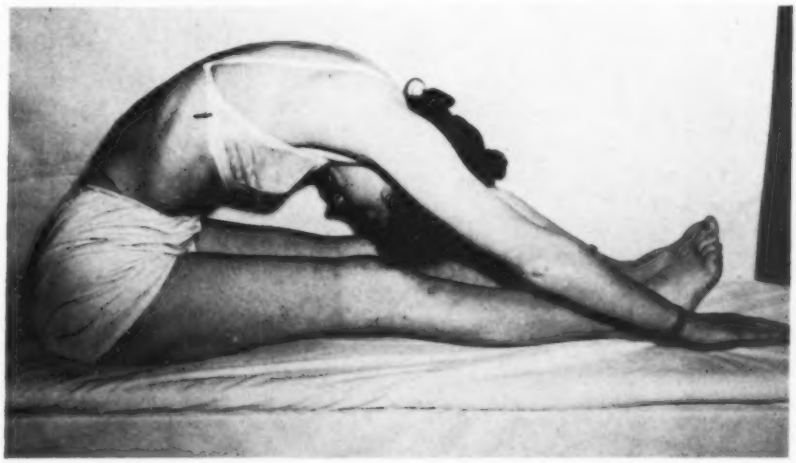

Fig. 13.—Case 20.

Laboratory Findings.—Laboratory findings disclosed hemoglobin, 13 grams per cent with 4.5 millions erythrocytes per cubic millimeter; leucocyte count, 11,000 per cubic millimeter with 47 per cent polymorphonuclear neutrophiles, 42 per cent small lymphocytes, 8 per cent monocytes and 3 per cent eosinophiles. Urinalysis was normal.

A diagnosis of acute anterior poliomyelitis was made and the patient given orthodox therapy.

Course in Hospital.—The course of treatment with results was as follows:

Oct. 26, 1941, There was almost complete flaccid paralysis of the right leg, and scattered weakness in the remainder of the right lower extremity. A splint was applied posteriorly from the heel to midthigh. The rest of the body was immobilized with sandbags, except for the arms.

Nov. 4, 1941. There was no change in the right lower extremity except for some improvement in flexion and extension of the toes. There was no further evidence of paralysis.

Nov. 18, 1941, Contraction of both glutei maximi was incomplete. Internal rotation of the right thigh was incompletely carried out.

Nov. 21, 1941, The patient was examined by Sister Elizabeth Kenny who found spasticity of the neck muscles, spasm of diaphragm and anterior tibial group on right, in addition to "alienation" of right biceps femoris and gluteus maximus. There was slight spasm of the left iliocostal muscles.

Dec. 1, 1941, Slight contraction of glutei was elicited.

Dec. 18, 1941, Weakness in affected muscles was lessening.

Dec. 21, 1941, The patient was discharged for transfer to another institution.

Fig. 14.—Case 19.

Fig. 15.—Case 19.

Progress.—Progress after leaving our hospital was recorded as follows:

From Feb. 2, 1942, until Sept. 15, 1942, the patient received the usual orthodox treatment for poliomyelitis at another hosptial, being kept on a Bradford frame for several months.

On Sept. 15, 1942, he was allowed out of bed using a right hip brace, and was permitted to become more active gradually until his discharge on April 15, 1943. (Fig. 14.)

He was admitted to our Kenny outpatient department on May 18, 1943, at which time the following findings were recorded: (1) Sternomastoids "alienated"; (2) "Cupping" of both shoulders; (3) Thoracic cage flaring at attachment of diaphragm; (4) Right scoliosis and slight kyphosis of thoraco-lumbar spine; (5) Right lower extremity: "alienation" of anterior tibial group of muscles; foot everted and externally rotated; weak dorso- and plantar flexion; "alienation" and atrophy of gluteus maximus and biceps femoris; (6) Patient walked with limp of right hip.

Following admission to our clinic the brace was at once removed and the patient started on muscle re-education exercises.

June 28, 1943, Considerable improvement was noted, especially in walking without the brace. The shortening of the cervical muscles and the spasm thereof persisted. Prostigmine therapy was initiated, using 1.0 mg. prostigmine methylsulfate subcutaneously with $\frac{1}{150}$ grain atropine sulfate daily.

July 2, 1943, Parenterally administered prostigmine methylsulfate was discontinued. Fifteen milligram prostigmine bromide was given orally four times daily.

July 22, 1943, All prostigmine therapy was discontinued. Unusual improvement had been noted. There was complete relaxation (to normal) of the cervical and paravertebral muscles and the "alienated" muscle groups of the right lower extremity had regained some function. (Fig. 15.)

DISCUSSION

It becomes readily apparent from a cursory review of the case histories and Table I that the most disturbing element which is encountered by the clinician treating poliomyelitis is the so-called muscle spasm. This has recently been thoroughly reviewed by Kabat and Knapp[6] who cited evidence that the pathologic basis for the condition is an internuncial lesion of the gray matter of the spinal cord. According to this concept the muscle spasm occurs as a result of release of proprioceptive reflexes from inhibition.

This, however, does not fully explain the effectiveness of prostigmine in relieving this spasm. This drug is well known and universally accepted as a parasympathicomimetic agent. Were this the only action of the substance, one might expect little or no skeletal musculature relaxation. Kremer[7] showed that the intrathecal administration of prostigmine to an individual having a hemiplegia resulted in a decreased tone of the muscles and reflexes effected by means of a direct action on the spinal cord. That the drug's parasympathicomimetic action is not responsible for its effect in cases of poliomyelitis can be proved by the concurrent administration of atropine. The latter is known to abolish the myoneural action, yet the relief from muscle spasm is just as pronounced. Obviously a certain amount of prostigmine must find its way into the spinal cord where it exerts a direct action.

We are of the opinion that prostigmine is an effective substitute for the burdensome hot packs which heretofore have constituted one of the

mainstays of the Kenny method. No claim is made for prostigmine's value in completely replacing the Kenny method, for, as has been demonstrated, the processes of muscle re-education and exercise must be continued. However, the latter phases of treatment are comparatively simple and easy, once careful instruction has been assimilated by the attendant. The hot packs are a different matter for, even though the technique is mastered, the actual operation is time-consuming and costly. The latter is true in that the blanket strips which are used are quickly worn out. The labor necessary for the proper application of hot packs precludes their extensive use at the present time. It therefore behooves the modern clinician to employ a combination of prostigmine, muscle re-education and exercise as the most practical and efficient means to treat poliomyelitis.

It is believed that emphasis should be placed upon the fact that old, chronic cases of poliomyelitis with deformities and "paralysis" will in many instances respond just as efficaciously to this type of treatment. In order to prove our contention, a number of such patients (Table I) were carefully studied over a period of many months. In some instances we found that even though hot packs were properly applied for long periods of time, the relief of muscle spasm and therefore pain was not complete until prostigmine was administered. As an example, one patient (Case 7) was in a cast for four months, and the parents informed by a reputable orthopedist that the child would never walk. However, following eleven months of the Kenny regime there was marked improvement, and after a short period of therapy with prostigmine the child walked without any aid. It has been noted repeatedly that one of the most encouraging effects of prostigmine is that it reestablishes coordination of muscles and makes the affected muscles more easily amenable to the muscle re-education.

It is our intention to treat the majority of patients in the future at home, using the modified Kenny technique with prostigmine. The present war has precipitated an acute, as yet unrelieved, shortage of physicians, nurses, technicians, and hospital beds. We advocate a short period of hospitalization to observe the extent of the disease process. Only those cases requiring considerable medical and nursing attention (such as those of the bulbar variety) need be hospitalized for long periods of time. It is estimated that at least 75 per cent of the patients can be adequately cared for at home. All patients will be carefully followed up over many months to be certain of their progress and be able to detect any recurring spasm or incoordination of muscles.

The development of myocardial lesions in poliomyelitis, secondary to the general toxic state, is very rare. That such probably never occurred in our cases is evidenced by an examination of the electrocardiograms which were taken (Table II). In several instances there was more than one tracing taken, the second usually being obtained after prostigmine had been administeerd. The absence of change from

TABLE II

INITIALS	AGE	SEX	TYPE OF POLIO.	ONSET	EKG. (DATE)	VENTRICULAR RATE/SEC.	PR INTERVAL (SECONDS)	QRS INTERVAL (SECONDS)	ST SEGMENT	T WAVE
A. B.	8	M	P	9/22/40	11/ 2/43	100	0.16	0.08	Normal	T_3T_4 inv.
A. B.	8	M	P	9/22/40	3/ 6/44	105	0.16	0.08	Normal	T_3T_4 inv.
J. L. M.	15	F	P	7/ 7/41	10/20/43	66	0.20	0.08	Normal	Upright
J. L. M.	15	F	P	7/ 7/41	3/ 1/44	64	0.17	0.09	Normal	Upright
R. B.	2	M	P	9/ 2/41	11/ 6/43	110	0.12	0.06	Normal	T_4 inv.
D. R.	5	M	P	10/12/41	3/ 4/44	120	0.17	0.07	Normal	T_3 inv. T_4 diphasic
F. R.	10	M	P	10/18/41	3/11/44	70	0.16	0.08	Normal	Upright
J. van P.	16	F	P	10/12/41	3/ 4/44	80	0.15	0.09	Normal	Upright
D. C.	5	M	P	10/19/41	10/20/43	96	0.16	0.08	Normal	T_3 low T_4 inv.
G. R.	8	F	P	7/ 4/42	11/16/43	84	0.15	0.09	Normal	T_3 diphasic T_4 inv.
G. J.	31	M	P	7/26/42	1/26/44	86	0.16	0.08	Normal	Upright
G. J.	31	M	P	7/26/42	3/ 1/44	72	0.16	0.09	Normal	Upright
M. S.	5	M	P	8/17/42	10/28/43	114	0.12	0.08	Normal	T_3T_4 inv.
N. N.	13	F	BP	9/25/42	10/30/43	120	0.15	0.08	Normal	T_3 inv.
J. B.	14	M	BP	9/26/42	11/ 4/33	80	0.15	0.07	Normal	T_3 inv.
J. B.	14	M	BP	9/26/42	3/22/34	108	0.16	0.08	Normal	T_3 inv.
J. B.	14	M	BP	9/26/42	9/18/35	108	0.16	0.08	Normal	T_3 inv.
J. B.	14	M	BP	9/26/42	1/16/36	84	0.14	0.07	Normal	T_3 inv.
J. B.	14	M	BP	9/26/42	9/11/36	90	0.12	0.08	Normal	T_3 inv.
J. B.	14	M	BP	9/26/42	10/23/43	92	0.16	0.08	Normal	T_3 inv.
J. R.	7	M	P	10/ 1/42	11/13/43	114	0.12	0.06	Normal	T_3T_4 inv.
D. H.	4	M	NP	10/15/42	11/13/43	126	0.14	0.06	Normal	T_3T_4 inv.
B. H.	12	F	NP	10/22/42	11/13/43	90	0.16	0.06	Normal	T_3T_4 inv.
J. B.	7	M	NP	10/ 7/42	12/ 2/43	124	0.14	0.06	Normal	T_3 flat
P. P.	5	F	P	8/25/43	11/27/43	116	0.12	0.06	Normal	Upright
P. P.	5	F	P	8/25/43	2/ 3/44	96	0.13	0.06	Normal	Upright
L. M.	5	M	P	8/18/43	11/27/43	136	0.12	0.06	Normal	Upright
G. N.	9	M	P	8/26/43	11/28/43	110	0.16	0.08	Normal	T_3T_4 inv.
G. N.	9	M	P	8/26/43	3/25/44	90	0.16	0.08	Normal	T_3 diphasic T_4 inv.
W. B.	8	M	NP	9/ 6/43	10/20/43	100	0.18	0.08	Normal	T_3 inv.
W. B.	8	M	NP	9/ 6/43	3/11/44	88	0.17	0.08	Normal	T_4 inv.
R. T.	15	M	P	9/16/43	11/27/43	94	0.14	0.08	Normal	Upright

P Paralytic
BP Bulbar paralytic
NP Non-paralytic

the first tracing is taken as evidence that prostigmine induces no cardiac changes demonstrable clinically or by electrocardiography. This should allay the fears of a few clinicians who still believe prostigmine exerts an effect upon the normal heart when it is given in therapeutic doses.

SUMMARY AND CONCLUSIONS

1. Twenty-one cases of acute, subacute, or chronic poliomyelitis are presented. All patients were subjected to a modified Kenny treatment with prostigmine following various forms of previous therapy. Each patient, therefore, was his own control.

2. The results obtained with prostigmine, muscle re-education and exercise are highly encouraging. We urge an extension of this method of therapy, especially in chronic cases.

3. Prostigmine was well tolerated in most instances, and there were no side effects demonstrable.

4. Approximately 75 per cent of patients with poliomyelitis can be adequately cared for at home without special nursing attention with this technique.

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GOAT'S MILK ANEMIA

Report of a Case

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RECENTLY an infant, 4 months old, suffering from goat's milk anemia, was admitted to the Rutland Hospital. We were able to find very little either in textbooks or journals about this condition. Because of the scarcity of material on this subject, we thought that this case history might be of interest.

N. H., born Nov. 4, 1943, was admitted to the Rutland Hospital March 2, 1944, with the complaint that she had been vomiting mucus with her feedings for two or three weeks, was pale, and failed to gain weight. Two weeks before admission, the baby was reported to have weighed about 11 pounds. She weighed 10 pounds, 5 ounces on admission. The baby's birth had been normal; the birth weight was 7 pounds, 6 ounces. She had been breast fed for twelve days after birth; then she was put on a formula consisting of goat's milk, Karo, and honey.

The mother reported that the baby had impetigo in the hospital following her birth. It was acquired when she was 2 or 3 days old and was not cleared up until she was 2 months old. It was treated with 50 per cent alcohol and ammoniated mercury ointment. At two months of age she had "canker." There was a white coating on the mouth, also red areas which bled easily. This was reported to have been treated with "gold thread" without result. It was then treated with boric acid mouth washes and cleared in about six weeks.

The family history was irrelevant except for the fact that all of the family used goat's milk instead of cow's milk, since they owned a herd of goats. Two siblings were alive and well.

The physical examination on admission showed a well-developed, poorly nourished white female infant, 4 months old, very pale, alert, with a shrill cry. The skin was dry and pale; the lips and tongue, dry. The chest was well shaped; the lungs, normal to auscultation and percussion; the heart sounds, normal with no murmurs. The abdomen was soft; the liver and spleen, not palpable. There was no edema of the extremities. The temperature was 99° F.

The laboratory findings were as follows: erythrocytes, 2,730,000; hemoglobin, 71 per cent; leucocytes, 8,300; polymorphonuclears, 31 per cent; lymphocytes, 69 per cent. Urinalysis on March 7, five days after admission, showed albumin, 3 plus; acetone and sugar, negative; microscopic examination, negative except for amorphous urates.

The treatment was as follows: For the first week, March 2 to March 9, treatment consisted of a formula of cow's milk, water, and Karo; cod liver oil; orange juice; Eisenzucker, 5 gr., three times daily. The orange juice was later discontinued because of vomiting, and cevitamic acid was substituted.

For the second week, March 9 to March 16, the following data were recorded: On March 9 the stools showed marked improvement with no

mucus. The baby was still vomiting. The hemoglobin had dropped from 71 to 56 per cent and the erythrocytes had dropped from 2,730,000 to 2,490,000. Blood smear showed one nucleated red cell, variation in the size and shape of the red cells but very little achromia. On March 10, lactic acid was added to the formula. On March 11, 80 c.c. of whole blood was given intramuscularly. Liver soup, 2 oz. daily, was started.

For the third week, March 16 to March 23, we noted the following: On March 16 the baby's weight showed a gain of 7 ounces. There was a further drop in hemoglobin to 54 per cent, and in erythrocytes to 2,200,000. Liver extract, ½ c.c. intramuscularly, was started. At first it was given daily; then, every second day; later, every third day. On March 18 the hemoglobin was 57 per cent; erythrocytes, 2,570,000. On March 22 it was noted that the baby's color was much better and that she was more active. Her hemoglobin was 80 per cent; erythrocyte count, 3,060,000.

For the fourth week, March 23 to March 29, improvement was marked. On March 24 the appetite was good, the baby was gaining steadily; hemoglobin was 81 per cent; erythrocytes, 3,820,000, with slight tendency toward macrocytosis and polychromatophilia. On March 29, thirteen days after the institution of liver therapy intramuscularly, the baby was discharged from the hospital. At that time, she had gained 1 pound and 2 ounces. The hemoglobin was 84 per cent and the erythrocyte count, 3,900,000. Urinalysis was negative.

There seem to be marked differences of opinion regarding the characteristics, causes, and proper treatment of this form of anemia. Our experience with this one case would seem to be in accord with the brief comments of Griffith and Mitchell,[1] quoted as follows:

> "Feeding with goat's milk may produce a severe hyperchromic, pernicious-anemia-like blood picture (goat's milk anemia) the cause of which is controversial; but apparently the anemia is not due to lack of iron alone, and possibly operative may be the action of fatty acids in the milk on the blood-forming tissue in the bone marrow. Liver or liver extract and iron are prophylactically and therapeutically effective."

This view of goat's milk anemia is in accord with the findings of Professor Rominger, director of the university children's clinic in Kiel, as reported by the regular correspondent of *The Journal of the American Medical Association* in Berlin in 1933. This report is taken from the issue of The Journal for Dec. 30, 1933.

> "Professor Rominger, director of the university children's clinic in Kiel, has begun a research on the pathogenesis and therapy of anemia due to the use of goat's milk. On the basis of comprehensive studies on metabolism in healthy and sick children who were nourished with goat's milk, and observations in animal experiments, he discussed the question as to whether anemia due to goat's milk is the result of a trophotoxic

> or a trophopenic injury. Clinical observations show that it is at least improbable that goat's milk as such has any toxic qualities. Feeding experiments on young growing white rats led to the conclusion that an exclusive diet of cow's milk produces an anemia of the chlorosis type (hypochromic anemia) which is evidently due to lack of iron, since it can be both prevented and cured by the administration of iron. An exclusive diet of goat's milk produces in very young rats an anemia of the pernicious type (hyperchromic anemia). This experimental hyperchromic goat's milk anemia cannot be cured solely by the administration of iron; nor is it due to lack of vitamin C. Furthermore, it can neither be produced nor exacerbated by the administration of unsaturated volatile fatty acids of goat's milk. It can, however, be prevented and cured by the injection of liver extracts. It is a complex deficiency disease, in which the factor that counteracts any tendency to perniciousness—namely, the so-called extrinsic factor—is absent, and likewise iron. The good effects of a combined liver extract and iron therapy were observed by Rominger. Within four weeks, therapeutic results could be secured such as were obtained with the former therapy, even along with the applications of blood transfusions, usually only after several months. . . . From the standpoint of prophylaxis, the use of goat's milk without the addition of liver and iron, must be avoided; but if these additions are made, there is no objection to goat's milk in the diet of infants. It may be mentioned that goat's milk contains more copper than other kinds of milk."

Other investigators who have studied experimentally produced goat's milk anemia in young rats, have reached quite different conclusions. Beard and Boggess, from the Department of Biochemistry, Louisiana State University Medical Center, New Orleans, in 1935, reported that:

> "The pathological findings in experimental goat's milk anemia are not similar to those in pernicious anemia of man, and any close relationship between both types of anemia must be denied. . . . Iron, with or without copper, prevented the onset of goat's milk anemia."

Other American investigators, studying experimental goat's milk anemia in young rats, have reached similar conclusions.

In our one case of goat's milk anemia in an infant, the lack of response to iron, diet, and transfusion therapy, and the dramatic response to liver extract intramuscularly would seem to indicate that in this case, at least, the required factor was in the liver, not in the iron. It would be interesting to know the experience of other clinicians with this type of anemia in infants.

Grateful acknowledgment is made to Drs. W. P. L. McBride, Louis Benson, and Louis Esposito for their help and interest in this case.

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CONGENITAL LUNG CYST COMPLICATED BY PYOPNEUMOTHORAX

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Raleigh, N. C.

AS THE condition congenital cystic lung disease is becoming more widely known, more cases are constantly being recognized. However, it is enough of a rarity to warrant the reporting of an additional case.

The literature has been reviewed several times recently[1, 3, 4, 10-12] and very excellent accounts are given as to the etiology, classification, symptomatology, and treatment of the disease, so these will not be reviewed here. It should be emphasized again, however, that this condition must be seriously considered in the differential diagnosis[9] of lung pathology, especially in pediatric practice. In any child or adult with a spontaneous pneumothorax[2, 5, 8] congenital cystic lung disease must be considered as a possible etiologic factor, and it must also be considered as a possible cause in dealing with lung emphysema,[7] lung abscesses, and in the differential diagnosis of solid tumors of the lung.[6]

REPORT OF A CASE

The patient, B. P., a 2½-month-old Negro male, was admitted to the Saint Agnes Hospital at 7:45 P.M. on Nov. 10, 1943, with the story that he had been perfectly well until approximately thirty minutes before admission. At this time the mother was preparing to feed him, when suddenly he "started to choke," even though no feeding had been given. "He turned very red and began to cry loudly." The crying continued constantly, his breathing began to be quite labored, and his color became "quite pale." He was taken directly to the hospital and admitted.

Past History.—He was born without difficulty in the same hospital. He weighed 6 pounds and got along well after birth with no difficulties except for mild pylorospasm, which was easily controlled with atropine. Since discharge he had done well with adequate feedings and adequate orange juice and cod-liver oil until the onset of the present illness.

Physical Examination.—His weight was 4.5 kg.; his temperature was 101.6° F., his respirations, 50. He was well developed and well nourished but was in obvious respiratory distress, with a rapid, grunting type of respiration. The skin was hot and wet. The positive physical findings were limited to the chest. The right chest appeared larger than the left and showed a definite respiratory lag. The heart was shifted to the left, the rate was rapid, and the rhythm, regular. Percussion note over the entire right chest was hyperresonant and the breath sounds were extremely faint over the corresponding area.

Course.—As the baby became quieted, the respirations became easier. It was felt that he had a spontaneous pneumothorax and sulfadiazine was begun prophylactically, 0.17 Gm. per kilogram of body weight, per twenty-four hours.

The laboratory work on the following day showed: Red blood count, 3.67 million, white blood count, 33,750; hemoglobin, 61 per cent; tuberculin, negative; and Wassermann, negative. A chest roentgenogram taken thirty-six hours later (Fig. 1) showed a right-sided pneumothorax, with the heart shifted to the left, evidence of fluid at the base, and a large cavity at the right apex, apparently in the substance of the lung.

During the next three days the patient seemed to improve gradually. His temperature remained at 100° F., he took his feedings fairly well, and his breathing became easier. However, on the fourth day, he suddenly began to breathe with very great difficulty, became ashen in color,

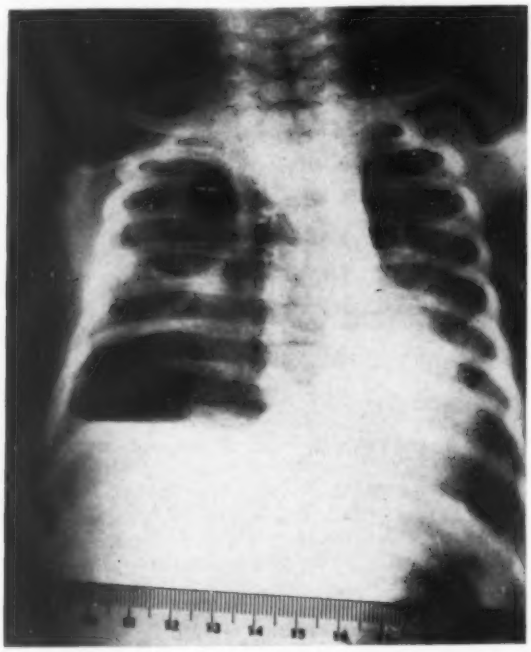

Fig. 1.—Roentgenogram taken Nov. 13, 1943, showing postero-anterior view of the chest.

went into shock, and became stuporous. A thoracentesis was immediately performed. A fair amount of air, which was under marked pressure, was removed, together with 40 c.c. of straw colored fluid, which when cultured revealed hemolytic *Staphylococcus aureus*. Respirations ceased and stimulants and artificial respiration were given. He rallied and the respirations again became easier and regular until he was quite comfortable.

Blood transfusions and fluids were given as supportive measures and the sulfadiazine increased to 0.26 Gm. per kilogram. On the sixth day, 40,000 units of staphylococcus antitoxin were given intramuscularly, and 20,000 units were given intramuscularly, on the following day. A marked improvement in this condition was noticeable the following

day and thoracentesis at this time revealed thick bloody pus, from which hemolytic *Staph. aureus* was again isolated. On the ninth day generalized edema was noticed with oliguria, the urine being loaded with sulfadiazine crystals. Sulfadiazine was stopped for thirty-six hours and parenteral fluids administered until the urinary flow was again well established, when the sulfadiazine was again begun.

On the eleventh hospital day, a closed drain was inserted in the right chest between the sixth and seventh rib in the posterior axillary line and very thick pus was obtained. Irrigations with azochloramine were begun twice daily. Following this there occurred a steady decrease in the amount of drainage, together with an increase in appetite, satis-

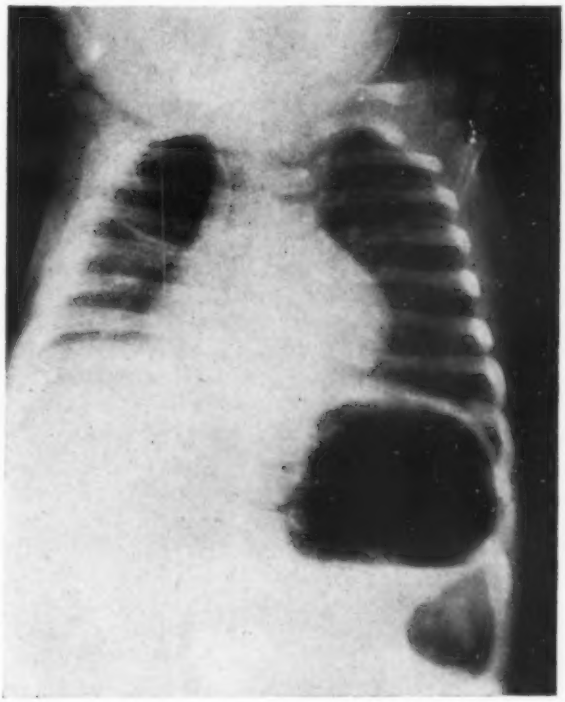

Fig. 2.—Roentgenogram taken Feb. 15, 1944, showing postero-anterior view of the chest.

factory weight gain, and some clearing of the chest as shown by roentgenograms, and physical examination. Sulfadiazine was discontinued December 10.

Two days later he began to cough persistently. This was associated with frequent vomiting, with the vomitus occasionally containing blood-streaked, purulent material. These symptoms became more persistent, although the irrigating fluid was changed to normal saline. A rapid weight loss ensued. A probable diagnosis of a bronchopleural fistula was made and as no improvement was seen, a rib resection was performed December 29, and open drainage of the right chest instituted.

Following this, there was a very rapid and satisfactory improvement. The cough and vomiting disappeared within a few days, the appetite improved, and he began to gain weight rapidly. There was a gradual diminution in the size of the cavity, together with a steady diminution in the amount of drainage.

On Feb. 1, 1944, after eighty-two days in the hospital, the patient was discharged with only a very slight discharge from the operative wound which two weeks later was found to be completely healed. The chest roentgenogram February 15 (Fig. 2) shows practically complete healing and closure of the empyema cavity. However, the cyst is still prominent at the right apex and seems to be unchanged in size or shape.

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THE LASHLEY QUADRUPLETS

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LOUISVILLE, KY.

IN LEITCHFIELD, Ky., on Feb. 23, 1941, at 8:30 A.M., the first of four babies was born to Mrs. Lashley without medical assistance. Mrs. Lashley, already the mother of eight other children, was in her seventh month of pregnancy. Dr. Tucker, the family physician, was soon summoned and arrived to find the firstborn, a girl, had a bleeding cord and considerable hemorrhage. He then delivered another girl at 10:30 A.M., followed by a boy at 12:15 P.M., and then another girl at 12:30 P.M. An incubator was secured by the County Health Nurse and the boy was placed in it since he appeared the weakest. The three girls were wrapped in blankets, warmed with hot water bottles, and placed in rocking chairs before a grate fire.

The attending doctor then summoned help from Louisville and an ambulance accompanied by the assistant resident in pediatrics and two nurses was immediately dispatched.

The ambulance arrived at 10:00 P.M. and all babies were found to be in good condition except the boy. He had marked respiratory difficulty and was given continuous oxygen. All were wrapped in blankets, and hot water bottles were used for heat.

They arrived at the Louisville City Hospital at 2:00 A.M. Monday, February 24, and were immediately placed in the premature room. Since the boy, John, was still having respiratory distress, glucose and saline were given subcutaneously and oxygen was continued. The following day he was given 100 c.c. of plasma intravenously. He gradually improved and thirty hours later the oxygen was discontinued.

Beulah, the firstborn, who had hemorrhaged at birth, had a red blood cell count of 3,600,000 per cubic millimeter and her bleeding and clotting time were prolonged, seven and five and one-half minutes, respectively. She was given 1 mg. of synkamin intramuscularly and a transfusion of 100 c.c. of plasma intravenously; and several days later, a blood transfusion.

The other two girls, Martine and Mildred, were in excellent condition.

After six days in the premature room at the Louisville City Hospital, the quadruplets were transferred to the premature room at the Norton Memorial Infirmary. The temperature in the premature room at both the City Hospital and the Norton Infirmary was kept at 90° F., and the humidity at 50 per cent. The babies were kept in the premature room at Norton Infirmary until they weighed 5½ pounds. At this point they were 6 weeks of age and had a stabilized temperature and

From the Department of Pediatrics, University of Louisville School of Medicine.
This study was aided by a grant from the Carnation Milk Co.

respiration. They were then transferred to the newborn nursery which maintained a temperature of 80° F.

The babies were given 5 c.c. of breast milk every three hours day and night. This was increased 5 c.c. every day until they were getting

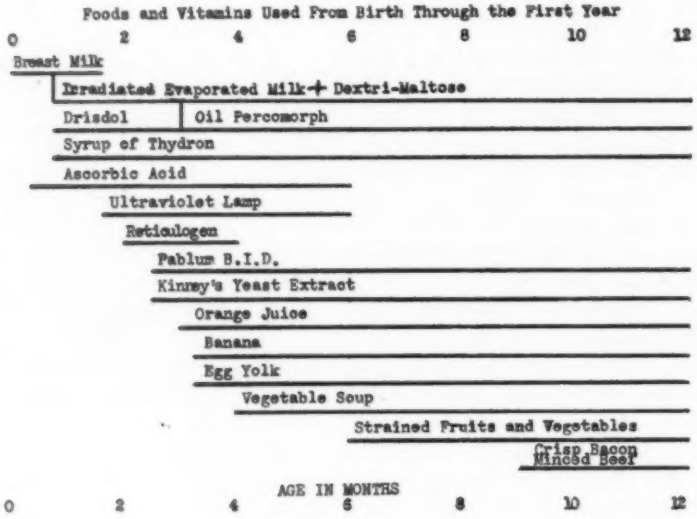


Fig. 1.

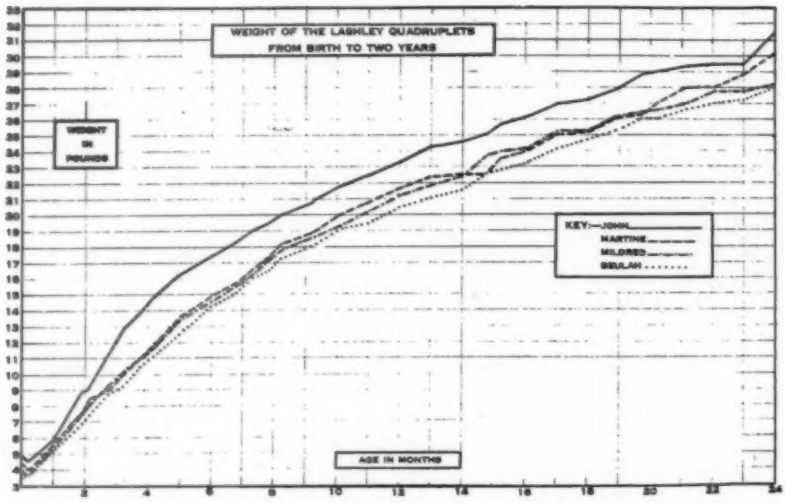


Fig. 2.

sufficient breast milk to gain weight. During this early period, and until they were 1 month of age, they were fed entirely by gavage. On March 17, when the babies were 22 days old, a formula of irradiated

evaporated milk and Dextri-maltose was added to their breast milk. This was gradually increased until April 15, when they were about 7 weeks old, they were placed entirely on the formula.

Ascorbic acid (25 mg. tablets) was added to the milk when the babies were 11 days old, and this amount of vitamin C was later increased to 50 mg.

Since premature infants and those of multiple births are very susceptible to rickets and anemia, 20 drops of Drisdol were added to the formula at 3 weeks of age. At the same time iron in the form of Syrup of Thydron was added to the formula. Beginning with 1 teaspoonful daily, this was increased to 2 teaspoonfuls two weeks later.

Ultraviolet rays were started at 7 weeks of age and were given three times a week as long as the children were in the hospital (six months).

At 2 months of age further fortification against anemia was provided by the administration of ½ c.c. of Reticulogen intramuscularly every three days for two weeks and then once a week until the children were 4 months old, at which time it was discontinued.

Pablum was started at the 2½-month period, together with Kinney's Yeast Extract (vitamin B complex). Percomorph oil replaced the Drisdol when the children were 3 months old.

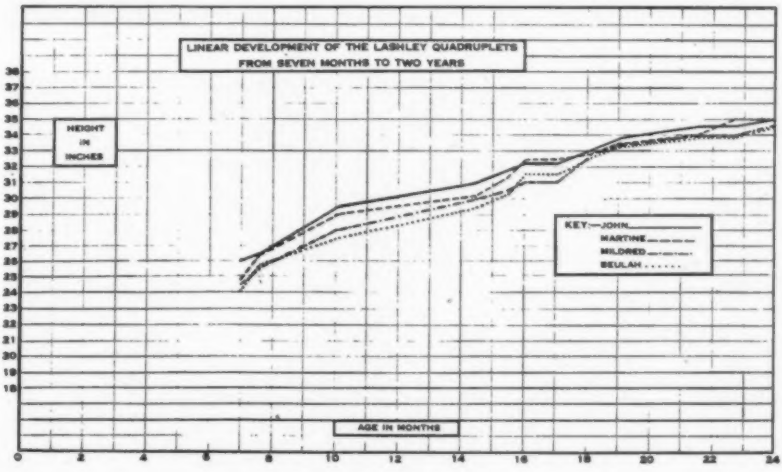


Fig. 3.

The various foods and vitamins used, together with their time of insertion in the diet of the Lashley quadruplets, are indicated graphically in Fig. 1.

Weights.—The weights of the babies at birth, six months later and at the end of one year are given in Table I.

The initial loss in birth weight was entirely regained by all the babies in two weeks. From this point on their weights steadily increased, placing them on a par with normal-term babies at the end of the first twelve

A.

B.

Fig. 4.

C.

D.

Fig. 4.—Cont'd.

TABLE I

	BIRTH WEIGHT	6 MONTHS	12 MONTHS
John	4 lb., 13 oz.	17 lb., 6¼ oz.	23 lb., 4 oz.
Martine	4 lb., 6 oz.	14 lb., 14 oz.	21 lb., 11 oz.
Mildred	3 lb., 14 oz.	14 lb., 10 oz.	21 lb., 4 oz.
Beulah	3 lb., 9 oz.	14 lb., 4 oz.	20 lb., 6½ oz.

months. The weights of the individual babies over a two-year period are illustrated in Fig. 2. The weight development of these quadruplets is within the normal range reported for normal-term male infants fed on irradiated evaporated milk.*

Linear Development.—The linear development of these children from 9 months of age through 2 years is indicated in Fig. 3. Their heights are also in the high normal range.

Blood Cytology.—Blood cytology has been carefully followed to measure the adequacy of the iron supplements to the diet.

Mildred Beulah John Martine

Fig. 5.

The bony development of the Lashley quadruplets has been good. There are no signs of rickets clinically or radiologically (Fig. 4, *A*, *B*, *C*, *D*). There is some variation in the degree of bone development in these four children. All but Martine have three well-developed centers of ossification in each carpus. Martine has two well-developed carpal centers and one which is barely visible. Beulah and Mildred have cen-

*Rhoads, T. F., M.D., Rapoport, M., M.D., Kennedy, R., and Stokes, J., Jr., M.D.: J. Pediat. 19: 169, 1941.

ters of ossification at the proximal ends of all the phalanges of both five digits. Martine apparently has these centers also, but the ones for the middle phalanges are extremely small. John has no centers of ossification at the ends of both distal and middle phalanges of both five digits. These variations in bone development are scarcely of any clinical significance, but are of interest.

Dentition.—Their tooth structure, according to their dentist, is excellent, superior to that of a comparable number of children who might be selected at random. All have a full complement of deciduous teeth, and there is no evidence of caries. The gum tissues are all normal, pink and firm, giving a clean healthy mouth appearance. The occlusion ranges from normal to excellent in all children.

A recent picture of the Lashley quadruplets is presented (Fig. 5). The similarity in gross appearance between Mildred and Beulah and John and Martine leads one to the belief that they are two sets of twins. The hair and skin of John are similar to Martine's. The spacing of John's anterior teeth is the same as that of Martine. Moreover, there is marked similarity of jaw structure between Mildred and Beulah. The latter two girls are identical twins.

The Lashley quadruplets were vaccinated for smallpox and inoculated for diphtheria. Following this Sauer's Pertussis Vaccine was administered. All members of the family were included in this program.

DISCUSSION

The conditions surrounding the birth of the Lashley quadruplets, their immediate postnatal care, feeding and the various factors which measure the adequacy of the diet, such as growth, height, bony development, and dentition are indicated. The children have been remarkably free of infection, and gastrointestinal upsets have been rare, indeed.

It has been a singular and interesting experience to be closely associated with the development of these quadruplets. Certain data concerning their development are herein recorded with the hope that they will be of interest to others.

CONCLUSION

Observance of the fundamentals of premature care, diligent and faithful nursing, immunization, an adequate and safe dietary, and family cooperation have resulted in the successful raising of Kentucky's only living set of quadruplets.

American Academy of Pediatrics

Proceedings

FIRST ANNUAL MEETING OF THE CUBAN BRANCH OF THE AMERICAN ACADEMY OF PEDIATRICS

HAVANA, AUG. 30, 1944

Cuban Branch Round Table Discussion on Region V

Chairman: Felix Hurtado, M.D.

Secretary: Emilio Soto Pradera, M.D.

Guests of Honor: Clifford G. Grulee, M.D., Secretary of the American Academy of Pediatrics, Evanston, Ill.
Angel Vieta, M.D., Dean of the Medical School, University of Havana.

Associates: Angel A. Aballi, M.D., Professor of Pediatrics, University of Havana, Cuba.
Clemente Inclan, M.D., Professor of Experimental Pathology, University of Havana, Cuba.
Julio Cabrera Claderin, M.D.
Carlos Hernandez Miyares, M.D.
Gabriel Gomez del Rio, M.D.
Agustin Castellanos, M.D.
Teodosio Valledor, M.D.
Serafin Falcon, M.D.
Roberto Valdes Diaz, M.D.
Gustavo Cardelle, M.D.

CHAIRMAN HURTADO.—This meeting and discussion were arranged to present the plan of the American Academy of Pediatrics for the admission of all the Latin-American pediatricians under the so-called Region V. Dr. Grulee was the colleague chosen by the executive committee to carry on this achievement. I deeply and sincerely wish to welcome Dr. Grulee in the name of all my colleagues of the Cuban branch. Dr. Vieta, dean of our medical school, has been very kind in allowing us to meet here this morning in one of the reception rooms of the University of Havana. Dr. Vieta wished also to welcome Dr. Grulee as a way of expressing the close relationship between Cuba and the United States of America.

DR. VIETA.—Dr. Hurtado was right when he took the liberty of expressing my own thoughts in regard to the meaning of this round table discussion. Before I leave this room I sincerely wish to welcome Dr. Grulee and I hope that, when he returns to the United States he will deliver a message of goodwill and friendship to his people.

DR. ABALLI.—It has been a great day because we are celebrating the entrance of our pediatricians into the American Academy of Pediatrics. I remember when a long time ago I proposed in one of the meetings of the Cuban Pediatrics Society the interchange of our Pediatric School and the American Academy of Pediatrics to strengthen the bonds of friendship between us by doing what has been fulfilled today. Cuba for many reasons has always been in close contact with all of you, "heart to heart," quoting Dr. Grulee. We have sent our youth to your country to get part of your culture, and many of our physicians have been graduated from American universities. My own son received most of his medical education from you. I wish now to speak about my beloved friend, Dr. Frederick Schlutz, who always treated my boy as a son. Dr. Schlutz was indeed one of the best in our Latin-American countries. He studied our language and deeply felt the influence of our friendship. I know he had always been one to urge the development of Region V, because he realized the future importance of this step, making it possible for us to know each other better so as to erase many mistakes born as the result of ignorance of Latin-American countries and their ways of thinking and living. I am quite sure Dr. Grulee will always have this group of Cuban pediatricians ready to help him sincerely, so that he can tell the executive board that at least in Cuba there is a branch upon which they can depend.

DR. GRULEE first of all thanked all of the members of the Cuban branch for their cooperation. He discussed the question raised by Dr. Hurtado concerning Region V, and emphasized that the American Academy of Pediatrics was not only willing to develop Region V with all the Latin-American countries, but also to allow this region to be represented on the executive board, although the way and extension of such an achievement had not yet been determined because the board did not know the desires of most of the Latin-American branches.

Furthermore, Dr. Grulee explained that Dr. Federico Gomez from Mexico and Dr. Hurtado from Cuba, were appointed to the meeting of the Academy in St. Louis, Mo., with the recommendation that they present a project to develop Region V, which later would be submitted to every Latin-American country for their consideration and further discussion. Dr. Grulee made it clear that he had not come because of any government pressure, but simply as a member of the executive board, willing to strengthen and make endurable our bonds of everlasting friendship. He mentioned the fact that he has been

traveling without priority since they did not want any government participation in this matter since their purpose was only the pure scientific interchange among all the pediatricians of this continent.

DR. HURTADO translated into Spanish Dr. Grulee's words which were fully approved by all the Cuban members of the branch. He made the remark that in all probability it would not be possible for him to reach St. Louis on time, because he has to accompany President Batista in his future trip to South America. Nevertheless, he could develop his plans for the constitution of Region V which in time would be delivered to the president of the Academy.

DR. GRULEE pointed out that in regard to Dr. Hurtado's inability to be present at the St. Louis meeting, it could be arranged to send Dr. Soto Pradera in his place. He would submit this matter to the executive board, with the understanding of its approval.

DR. HURTADO replied that this would be the best thing to do, since Dr. Soto Pradera has always been in close contact with Dr. Grulee and consequently with the American Academy of Pediatrics. Furthermore, Dr. Soto Pradera has helped him a great deal, making possible the constitution of the Cuban branch.

DR. GRULEE pointed out that we should limit the number of scholarships at present, until further arrangement could be made from the financial point of view. He made the remark that such temporary limitation was not the ideal of the Academy, that in the future it wanted to have as many Latin-American students as possible.

DR. HURTADO stressed the point that Cuban scholars would be chosen by our local committee and all of them would be well-trained pediatricians. The idea is to get students to learn some of the subjects in which we have no experience, as for example, research in some of the pediatric fields which we cannot possibly develop here. He also proposed that the fee of the Cuban fellows be raised to twenty dollars so as to improve the future economical conditions of the Academy. This point was approved by all the members with the hope that such a step could be taken by the rest of the Latin-American countries.

DR. SOTO PRADERA as secretary of the branch made a résumé of the meeting and submitted to all members for approval the points suggested by the chairman and Dr. Grulee, all of which were fully approved. Dr. Soto Pradera's words were as follows:

> The historical process of development of the Latin-American group to constitute Region V began after the Pan-American Child Congress held in the city of Washington in May, 1942, when the executive board of the American Academy of Pediatrics took up the question of creating memberships in the

Latin-American countries. We must say that since then, we are very much indebted to Dr. Clifford G. Grulee, whose proposal was approved by his colleagues.

Mexico was the first country selected by Dr. Grulee because of its proximity to the United States of America, the war being responsible for the lack of transportation which made such proximity all the more convenient. Nevertheless, immediately after this selection, we received an invitation to join the American Academy of Pediatrics, this invitation being extended to all Latin-American countries. In this way we are establishing the Cuban Branch. Dr. Hurtado was elected chairman, and Dr. Soto Pradera, secretary.

The local approval of this group was happily welcomed and accepted by most of the Latin-American countries. Now, we have only to decide how this Region V will work in the future. This decision is the reason Dr. Grulee asked Dr. Felix Hurtado and Dr. Frederico Gomez from Mexico, to be present at the annual meeting to be held at St. Louis, Mo.

Our meeting this morning constitutes the first step taken by us as a branch, taking the opportunity to submit to your consideration the following points:

1. To approve the designation of Dr. Hurtado as a member to organize the program for Region V, which will be submitted finally to the Latin-American group.
2. To approve the designation of a local committee for the selection of Cuban physicians asking for a scholarship in the field of pediatrics. This local committee would act only as an intermediary between the executive board and our group, the executive board having the final word of approval. The local committee would include Professor Aballi, Professor Hurtado, and Dr. Soto Pradera.
3. To approve the proposition of Dr. Hurtado concerning the future election to membership of the Cuban branch. This proposition having been established the election will take place every two years, the new members having fulfilled all the requisites already established by the board of the American Academy of Pediatrics.
4. Finally, to approve all that has been done already by our chairman and secretary since November, 1942, when the invitation to organize our branch took place.

DR. HURTADO finally proposed the nomination of Dr. Clifford G. Grulee and Dr. Henry Helmholz as honorary members of our Pediatric Society. The proposition was approved without discussion.

DR. VALLEDOR congratulated Dr. Grulee and Professor Aballi as president of the Cuban Pediatric Society for the election of these two

prominent pediatricians. He also congratulated the secretary of the branch for his devoted work and cooperation with all the rest of the Cuban fellows.

DR. GOMEZ DEL RIO as member of the executive board of the Cuban Pediatric Society supported Dr. Hurtado's proposition, stating that Dr. Frederick Schlutz had been elected honorary member some time ago after Professor Aballi's suggestion.

DR. SOTO PRADERA presented Dr. Hurtado's proposition concerning the future continental meeting of the Academy, which would afford the opportunity of discussing the definite position of Region V on the executive board, as what has been called the Latin-American Division by Dr. Hurtado. This meeting would be held in the city of Chicago at the end of the war under the auspices of the American Academy of Pediatrics.

The Pediatrician and the War

The following is a continuation list of Fellows of the American Academy of Pediatrics on active duty in the Military Services:

Army

Dr. G. D. Carlyle Thompson, San Francisco, Calif. (Major)

Navy

Dr. Anna L. Hays, Tulsa, Okla. (Lieutenant Commander, United States Naval Reserve)

The following Fellows of the Academy have been promoted since entering the Military Services:

Army

Major W. A. Howard, Washington, D. C., to Lieutenant Colonel
Lieutenant Colonel James G. Hughes, Memphis, Tenn., to Colonel

REPORT OF THE TREASURER OF THE AMERICAN ACADEMY OF PEDIATRICS

STATEMENT OF RECEIPTS AND DISBURSEMENTS

JULY 1, 1943, TO JUNE 30, 1944

Balance in checking account, July 1, 1943			$ 3,679.11
Balance in savings account, Initiation fees			8,018.08
Balance in savings account, International Congress			507.53
			$12,204.72
Receipts:			
Dues		$26,408.25	
Exhibits, 1944 meeting		4,267.50	
Initiation fees		2,500.00	
Interest earned		721.43	
Pamphlets, Child Health Record	$ 333.98		
Immunization Procedures	250.09		
Vitamins	11.20	595.27	
Subscriptions, Men in Service		490.83	$34,983.28
			$47,188.00
Disbursements:			
Annual meeting, 1944		$ 79.36	
Bank charge and exchange		78.61	
Certificates and mounting		111.10	
Executive board		2,453.72	
Miscellaneous		420.88	
Office supplies and equipment		160.06	
Postage		602.88	
Refund, initiation fee		25.00	
Rent		1,738.09	
Salaries, Secretary	$7,500.00		
Assistant secretary	600.00		
Stenographer	1,850.01		
Office	1,800.62	11,750.63	
Stationery and printing		1,593.02	
Subscriptions		6,919.65	
Telephone and telegrams		417.43	
Travel expense (Secretary)		157.68	
Treasurer's bond		92.50	
U. S. bonds purchased		7,000.00	
Expense, Regions		2,061.81	
States		276.92	
Committees		566.01	
Pamphlets, Child Health	$ 445.09		
Immunization Procedures	355.84		
Vitamins	.99	801.92	$37,307.27
Balance, June 30, 1944			$ 9,880.73
Balance in checking account, June 30, 1944			$ 5,810.69
Balance in savings account, Initiation fees			2,559.98
Balance in savings account, International Congress			1,510.06
			$ 9,880.73

News and Notes

The Directory of Medical Specialists

The following notice is published in response to many inquiries to assist those certified by the American Board now engaged in correcting their previous listings, or preparing new sketches for the third edition of the Directory to be published early in 1945.

The biographic data of the first two editions of the *Directory of Medical Specialists* included only positions (internships, residencies, or assistantships) held during the course of training of men up to the time of their certification by the American boards, and hospital and medical school staff positions then currently held.

It is desired to extend this data in the third edition to include all formal hospital and medical school appointments, with dates held, even though now resigned, as well as records of all military service including commissions and dates, either in World War I, peacetime in the reserve forces, or in World War II.

Thus, a chronologically complete sketch of a diplomate's entire career is to be included in this third edition of the Directory.

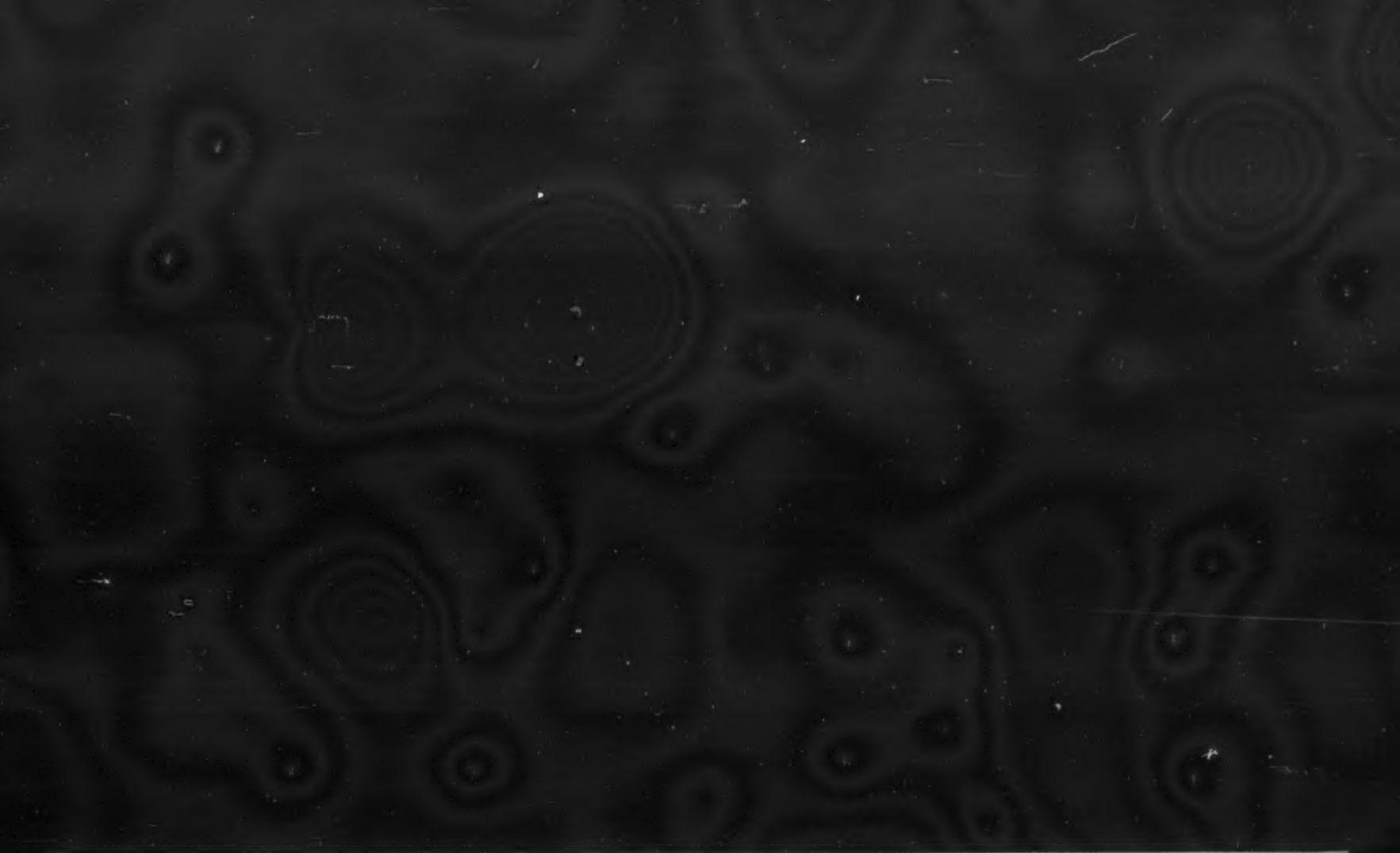
Membership or fellowship in national or sectional (not local) special societies, and national general societies with offices held, and dates in any of these should be reported.

Membership in recognized international medical societies may be included, but honorary or other membership in foreign medical societies should not be reported.

Reference to the second edition (1942) of the Directory may be made for lists of medical societies to be included in one's biographic sketch.

Families or secretaries of men absent in military service are asked to complete or correct previous listings or new forms now being mailed to those eligible for inclusion in the Directory. Only those certified by an official American Board can be included, and there is no charge for this listing.

Communications should be addressed to the Directory of Medical Specialists, 919 N. Michigan Avenue, Chicago 11, Ill.

Dr. Henry Helmholz of Rochester, Minn., and Dr. Clifford Grulee of Chicago, Ill., have been elected to honorary membership in the Cuban Pediatric Society.

Dr. Roger W. Dickson has recently been made Professor and Chairman of the Department of Pediatrics in the School of Medicine of Emory University and Chief of the Pediatric Service in Grady Memorial (Municipal) Hospital, Atlanta, Ga.